UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK
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YEDA RESEARCH AND DEVELOPMENT COMPANY LTD.,

Plaintiff,

OPINION AND ORDER

- against -

03 Civ. 8484 (NRB)

IMCLONE SYSTEMS INC. and AVENTIS PHARMACEUTICALS, INC.,

Defendants.

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NAOMI REICE BUCHWALD
UNITED STATES DISTRICT JUDGE

Plaintiff Yeda Research and Development Company, Ltd. ("Yeda") brought this action against defendants ImClone Systems Inc. ("ImClone") and Aventis Pharmaceuticals, Inc. ("Aventis") alleging improper inventorship of United States Patent No. 6,217,866 (the "'866 patent"). Yeda is affiliated with the Weizmann Institute of Science (the "Weizmann"), a world-renowned academic institute located in Rehobot, Israel, and exists to protect the intellectual property created at the Weizmann. Yeda is the assignee of the legal interests of three scientists employed at the Weizmann during the mid- to late- 1980s, namely Professor Michael Sela ("Sela"), Dr. Esther Aboud-Pirak ("Pirak"), and Dr. Esther Hurwitz ("Hurwitz") (collectively, the "Weizmann scientists"), who maintain that they are the true

inventors of the '866 patent. The legal rights of the scientists actually named on the patent, Professor Joseph Schlessinger ("Schlessinger"), Dr. Francoise Bellot ("Bellot"), Dr. Richard Kris ("Kris"), and Dr. David Givol ("Givol") (collectively, the "named inventors"), have been assigned to defendants Aventis and ImClone. The named inventors all worked at Meloy Laboratories, Inc. ("Meloy") and its successor corporation, Rorer Biotechnology, Inc. ("Rorer"), both predecessors-in-interest to Aventis, during that same time period. ImClone is the exclusive licensee of the patent at issue.

Yeda filed its complaint on October 28, 2003, seeking joint inventorship of the '866 patent. Subsequently, the Court granted leave for Yeda to amend the complaint to seek a judgment adding the Weizmann scientists to the patent and removing the named inventors. After we denied summary judgment to defendants, see Yeda Research and Develop. Co., Ltd. v. ImClone Sys. Inc., 03 Civ. 8484(NRB), 2005 WL 2923545 (S.D.N.Y. Nov. 3, 2005), the Court held a bench trial to determine inventorship; the trial began on June 5, 2006 and concluded with oral argument on July 19, 2006.[1] The opinion that follows constitutes this Court's findings of fact and conclusions of law.

[1] Due to scheduling conflicts, proceedings were held on June 5-8, and resumed on June 16-21. After allowing the parties time to prepare

SUMMARY

In the mid-1980s, Schlessinger left the Weizmann on a sabbatical, accepting a position at Meloy/Rorer. Soon thereafter, Schlessinger invited Drs. Givol, Kris, and Bellot, all colleagues from the Weizmann, to join him. Under Schlessinger's direction, the named inventors created two monoclonal antibodies[2] ("mAbs") for use as research tools. Subsequently, in January 1987, Schlessinger and Hurwitz had a brief discussion at the Weizmann, during which Schlessinger offered to give samples of the antibodies to the Weizmann scientists. Though both Schlessinger and Hurwitz recalled having this conversation, they provided different accounts of it during the trial. While Schlessinger offered a somewhat extended version of the conversation, Hurwitz testified that Schlessinger merely described the antibodies as "good" and did not suggest any intended uses.

The Weizmann scientists performed experiments with the antibodies for the next fourteen months. During that time, they discovered that when one of the two antibodies, known as mAb 108, was administered in vivo in a mixture with chemotherapy drugs, the effect on human tumor cells was synergistic; i.e.,

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proposed findings of fact and post-trial briefs, closing arguments were held on July 19.

[2] All relevant scientific terms are defined in the body of the opinion.

the combined effect exceeded the effect of the antibody alone added to the effect of the drug alone. Whether Schlessinger would have anticipated that the Weizmann scientists would conduct a mixture experiment was a matter of dispute during the trial. Schlessinger testified that he "knew" that this mixture experiment would be performed based on his knowledge of Hurwitz's prior work. Hurwitz, however, testified that most of her prior work involved testing conjugates, whereby one substance is chemically attached to another, rather than mixtures, which involve separately administering two substances that are not attached. In fact, Hurwitz testified that the Weizmann scientists only decided to conduct the mixture experiment more than a year after the research began, and only then as a result of Hurwitz's independent judgment that such an experiment might yield promising results.

Soon after the discovery of the synergistic effect, Drs. Sela and Pirak informed Schlessinger in March 1998 of their discovery of this synergy while Schlessinger was visiting the Weizmann to deliver a lecture. About a month later, Pirak sent Schlessinger a draft of a paper she was preparing summarizing the results of the experiments the Weizmann scientists' had conducted with mAb 108. Almost immediately thereafter, Meloy/Rorer began pursuing patent protection for both the antibodies themselves and for the method of administering them

with chemotherapy drugs that had been developed by the Weizmann scientists. Only the scientists employed by Meloy/Rorer were included as inventors on its patent applications. The Weizmann scientists were not included as inventors, even though they had conducted all of the experiments relating to the mixture of mAb 108 and chemotherapy drugs. Moreover, Meloy/Rorer and later, ImClone, directly copied the text and figures from the paper drafted by the Weizmann scientists into their patent applications.

On September 1, 1988, Meloy/Rorer filed the first application in the chain of applications that eventually led to the issuance of the '866 patent. During the patent application process, the Patent and Trademark Office (the "Patent Office" or the "PTO") repeatedly rejected claims drawn solely to the monoclonal antibodies themselves, finding them insufficiently distinct from prior art. The PTO also raised several questions about the fact that the patent application seemed to be drawn directly from work done by the Weizmann scientists. Defendants overcame this objection by suggesting that they had entirely conceived of the research conducted by the Weizmann scientists, who had simply followed their directions as to what experiments to perform. Eventually, in April 2001, the '866 patent issued.[3]

[3] The '866 patent contains nine claims:

1. A method for inhibiting the growth of human tumor cells that express human EGF receptors and are mitogenically-stimulated by EGF, the method comprising administering an effective amount of an anti-neoplastic agent to a human cancer patient having said tumor cells; (i) wherein said antibody binds to the extra-cellular domain of the human EGF receptor of said tumor cell; (ii) wherein the antibody is not conjugated to the anti-neoplastic agent; and (iii) wherein the antibody inhibit [sic] the binding of EGF to the EGF receptor.

2. A method for inhibiting the growth of human tumor cells that express human EGF receptors and are mitogenically stimulated by human EGF according to claim 1 wherein said anti-neoplastic agent is doxorubicin.

3. A method for inhibiting the growth of human tumor cells that express human EGF receptors and are mitogenically stimulated by human EGF according to claim 1 wherein said anti-neoplastic agent is cisplatin.

4. A method for inhibiting the growth of human tumor cells that express human EGF receptors and are mitogenically stimulated by human EGF according to claim 1 wherein said monoclonal antibody is 108 produced by hybridoma cell line ATCC HB 9764.

5. A method for inhibiting the growth of human tumor cells that express human EGF receptors and are mitogenically stimulated by human EGF according to claim 1 wherein said monoclonal antibody is further characterized by its capability to inhibit the growth of human oral epidermoid carcinoma (KB) cells by binding to the extra-cellular domain of the human EGF receptor of said KB cells in an antigen-antibody complex.

6. A therapeutic composition comprising an amount of monoclonal antibody and an anti-neoplastic agent effective to inhibit the growth of human tumor cells that express human EGF receptors and are mitogenically stimulated by human EGF in association with a pharmaceutical carrier; (i) wherein the antibody binds to the extracellular domain of the human EGF receptor of the tumor

The patent only included those claims drawn to the method of administering an antibody in a mixture with chemotherapy drugs; the PTO did not permit the antibodies themselves to be patented. In fact, the antibody that ImClone sells under the name Erbitux is not one of the antibodies created by the named inventors, but rather another member of the class of antibodies specified in the patent. This antibody was created before the named inventors created mAb 108.

Significantly, defendants did not inform either Yeda or the Weizmann scientists of their patent applications based on the work performed at the Weizmann. Yeda learned that defendants were seeking a patent in January 2000, twelve years after the initial patent application, and fourteen months before the '866 patent issued. Immediately after the patent issued, Yeda engaged in discussions with defendants in an effort to have the

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> cells; (ii) wherein the antibody is not conjugated to the anti-neoplastic agent; and (iii) wherein the antibody inhibits the binding of EGF to the EGF receptor.
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> 7. A therapeutic composition according to claim 6 wherein said anti-neoplastic agent is doxorubicin.
>
> 8. A therapeutic composition according to claim 6 wherein said anti-neoplastic agent is cisplatin.
>
> 9. A therapeutic composition according to claim 6 wherein said monoc+lonal antibody is 108 produced by hybridoma cell line ATCC HB 9764.

U.S. Patent 6,217,866.

Weizmann scientists added to the patent. While these discussions were ongoing, ImClone obtained FDA approval for the treatment of certain types of human cancer, permitting it to distribute Erbitux under the protection of the '866 patent. As of the date of trial, ImClone had received about $900 million in revenues under a distribution agreement with Bristol Myers Squibb.

The two primary issues now before this Court are: first, which scientists invented the subject matter of the '866 patent; and second, whether the affirmative defense of laches is available to defendants. In analyzing the inventorship issue, we focus on several subsidiary issues: (1) whether Schlessinger communicated a research protocol to the Weizmann scientists before they began their research; (2) to what extent Schlessinger conceived of the invention with the requisite definiteness; (3) to what extent the Weizmann scientists' prior research was predictive of the experiments relevant to this case; (4) whether the creation of the antibodies is sufficient in and of itself to entitle the named inventors to remain on the patent; (5) whether the named inventors and the Weizmann scientists determined that mAb 108 inhibits the binding of epidermal growth factor to its receptor; and (6) whether there exists any evidence of joint inventorship between the named inventors and the Weizmann scientists. In connection with the

laches defense, we focus on three issues: (1) to what extent the Weizmann scientists had knowledge that defendants were pursuing a patent; (2) whether the defendants acted deliberately in failing to disclose their actions; and (3) whether plaintiff was otherwise obligated to file its own patent application.

Having considered all of the evidence, we now find that the Weizmann scientists are entitled to sole inventorship of the '866 patent. In so holding, we make the following factual determinations, all of which are discussed at length infra: (1) Schlessinger did not give Hurwitz specific information regarding the properties of the antibodies or any intended uses; (2) Schlessinger did not specifically contemplate that the Weizmann scientists would perform the mixture experiment that forms the basis for the '866 patent; (3) the named inventors' creation of the antibodies used by the Weizmann scientists does not entitle them to inventorship; (4) the Weizmann scientists solely conceived of the idea embodied in the '866 patent; and (5) in light of the defendants' unclean hands, i.e., their copying from the Weizmann scientists' draft paper and their efforts to prevent Yeda from discovering defendants' patent applications, Yeda did not unreasonably delay asserting its rights relative to the '866 patent. Each of these conclusions is premised both on credibility determinations and the fact that while the

plaintiff's version of events is strongly corroborated by contemporaneous documents, defendants' version is not.

BACKGROUND

I. PARTIES

As noted earlier, plaintiff Yeda is an independent entity affiliated with the Weizmann that exists in order to protect the intellectual property rights of the Weizmann, which Yeda accomplishes by, inter alia, seeking patents and licensing agreements. See David Mirelman ("Mirelman") Witness Statement ("WS") at ¶¶ 7-8.[4] As relevant here, Yeda owns any rights in the '866 patent claimed by the Weizmann scientists. See Dr. Haim Garty ("Garty") WS at ¶ 29. Under the terms of a team agreement signed in August 2002, the Weizmann scientists are entitled to forty percent of any royalties Yeda receives if it succeeds in this lawsuit. See id. at ¶ 31.

Also, as mentioned supra, defendant Aventis is the successor in interest to Meloy Laboratories, Inc. ("Meloy"), which was acquired by the Rorer Group in 1986 and became Rorer Biotechnology, Inc. ("Rorer"). See Dr. Alain Schreiber ("Schreiber") WS at ¶ 1. The named inventors of the '866

[4] The parties agreed before trial that the direct testimony for their non-adverse witnesses would be proffered by sworn affidavits. The letters "WS" will be used in our citations to refer to these witness statements.

patent, Drs. Schlessinger, Bellot, Givol, and Kris,[5] were all employed at Meloy/Rorer during the period relevant to this case. See generally Schlessinger WS; Bellot WS; Givol WS; Kris WS. At the time that the named inventors arrived at Meloy in 1985, Meloy's biotechnology center was deeply involved in cancer research and product development. However, when the Rorer Group took over Meloy shortly thereafter, its focus shifted away from cancer research and toward developing the Rorer Group's existing products, especially Maalox, and toward research in, inter alia, cardiovascular, respiratory, and gastrointestinal therapies. See Schlessinger WS at ¶ 12. In 1990, the Rorer Group merged with the health care arm of Rhone-Poulenc, forming Rhone-Poulenc Rorer, Inc. ("RPR"). Nine years later, RPR merged with Hoechst-Marion-Roussel to form Aventis. In 2004, Aventis was acquired by Sanofi-Synthelabo, forming the sanofi-aventis Group. Defendant Aventis Pharmaceuticals is a wholly-owned subsidiary of the sanofi-aventis Group. See Schlessinger WS at ¶ 13.

Defendant ImClone is a corporation organized under the laws of Delaware that maintains its principal place of business in New York. Stipulated Facts ("SF") at ¶ 3. ImClone is the

[5] The disputed patent also names George A. Ricca, Christopher Cheadle, and Victoria J. South as inventors. However, all parties agree that none of these scientists had any role in the invention at issue, which Aventis admitted in a Rule 30(b)(6) deposition prepared in connection with its earlier motion for summary judgment. See Stipulated Facts ("SF") at ¶ 5. The parties have agreed to amend the patent after the conclusion of this case to properly reflect this fact.

exclusive licensee of the '866 Patent pursuant to an agreement with RPR signed in June 1994. As part of that agreement, ImClone agreed to take over the prosecution of RPR's pending patent applications relating to the subject matter of this case, which eventually culminated in the '866 patent. See Thomas C. Gallagher ("Gallagher") WS at ¶¶ 4-5. Pursuant to the protection offered by the '866 patent, ImClone now sells Erbitux, a drug approved by the Food and Drug Administration ("FDA") for use in cancer therapy. See Ronald A. Martell ("Martell") WS at ¶ 3. Currently, Erbitux is ImClone's only commercially available drug. See id. at ¶ 16.

II. FACTS

Although many of the underlying facts in this case are not disputed, the Court was nonetheless compelled to make many findings of fact that hinge in large part on credibility findings. Having carefully considered all of the testimony and evidence, we have concluded that the plaintiff's witnesses were, as a whole, far more credible than the defendant's witnesses.[6] We emphasize that our credibility findings are in no way intended to impugn the professional reputations of the

[6] We exclude from this broad statement the testimony of the parties' expert witnesses, Dr. Stuart Aaronson and Dr. Marc Lippmann, both of whom possess extraordinary credentials and impressed the Court as truthful and credible in their testimony, even if they were not always in agreement with each other.

extraordinary scientists who testified at trial.[7] We also note that, although the Weizmann scientists have a financial interest in the outcome of this case, while the named inventors do not,[8] all the scientists who claim inventorship of the '866 patent seemed entirely motivated by their desire to be recognized for their professional accomplishments, rather than by any financial interest.[9] Our bases for finding certain witnesses credible and others not are discussed throughout the opinion.

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[7] It is indeed an unfortunate circumstance that the Court ever had to be called upon to make and publish such credibility findings. As I noted at the end of closing arguments:

> I would like to state on the record that regardless of the decision I reach, it has really been a highlight for me to have as many dedicated and distinguished scientists in my courtroom . . . . [I]t was a professional pleasure for me to meet, even in this formal setting, scientists who are engaged on a daily basis in work which has already had so much benefit for human kind.
>
> As judges, we hear a great deal of testimony about nonproductive, if not criminal, activity for which we can have no gratitude. It is a welcome change of pace to hear testimony from people, and I mean this on both sides of the case, who are making such exceptional and positive contributions for the benefit of all of us.

Tr. 1560 lines 12-25.

[8] However, it was suggested at trial that Schlessinger's former affiliation with the Weizmann might entitle him to some share of the royalties if plaintiff prevails.

[9] Particularly noteworthy was Professor Sela's testimony that if he were applying for the same patent today, he would "of course" include Schlessinger on the application. Sela explained:

A. Terms and Definitions

1. Antibodies

Before proceeding with a detailed discussion of the events underlying this lawsuit, a brief summary of the relevant terms and definitions is appropriate.[10] First, an antibody is a "protein produced by the immune system of humans and other higher animals in response to the introduction into the body of a foreign antigen, which is almost always a protein." Expert Report of Dr. Marc E. Lippmann, M.D. ("Lippmann Report") at 4. Antibodies consist of four polypeptides, or chains of amino acids: two long polypeptides (the "heavy chain") form a Y-shape, while two short polypeptides (the "light chain") attach to the heavy chain, forming the structure depicted below. See id. Each branch of the "Y" contains a specific site where the antibody recognizes its corresponding antigen. These antigen recognition sites vary from antibody to antibody, and are thus

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> I must say personally, this may not be correct in terms of the law, but I have never been for removing people. I have been always the more the merrier, having a great group. That's why I always had so many collaborators on the papers. In view of the history of the patent, now I realize it was given only for the combination, and the combination was entirely our idea.

Tr. 262 lines 11-17.

[10] Although this section largely is derived from the expert report of Dr. Marc E. Lippmann, M.D., a plaintiff's witness, there is no dispute as to the definitions provided herein. We rely on Dr. Lippmann's report simply because he most clearly sets forth in writing the scientific underpinnings of the instant dispute.

referred to as the "variable region." See id. On the other hand, the base of the "Y" is the same for each class of antibodies and is referred to as the "constant region." See id.

The blood of humans and other animals "contains innumerous antibodies circulating, each recognizing the various antigens that have invaded the body." Lippmann Report at 6. In order to create antibodies for use in their research, scientists inject immunized animals with an antigen, triggering the animal to produce antibodies against the antigen. See id. Scientists then draw the animal's antibody-rich blood, which is referred to as antiserum. See id. The antibodies harvested in this manner are referred to as polyclonal antibodies. See id. at 6-7. Polyclonal antibodies have long been considered valuable research tools, limited by two factors: first, antisera contain antibodies specific to the injected antigen as well as

antibodies that are not antigen-specific;[11] second, polyclonal antibodies cannot be reproduced indefinitely, as antisera must be drawn from the blood of a live animal. See id. at 7.

The limitations of polyclonal antibodies were overcome in 1975, when Georges Köhler ("Köhler") and Cesar Milstein ("Milstein") developed technology for creating antibodies that are both antigen-specific and can be indefinitely reproduced, a discovery for which they were awarded the Nobel Prize in Medicine in 1984. See Lippmann Report at 7. These antibodies, known as monoclonal antibodies ("mAbs" or "monoclonals"), are created by immunizing a "nude" mouse[12] with a particular antigen, against which the mouse will generate antibodies. See id. at 8. The researcher then collects the B lymphocytes, which are the immune cells that produce antibodies, from the mouse's spleen. See id. In order to immortalize[13] these immune cells, the researcher fuses them with immortalized lymphocyte tumor cells. See id. The resultant cells, known as hybridomas, will produce a single type of antibody that will recognize only the antigen

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[11] As Dr. Hurwitz explains, "[p]olyclonal antibodies are essentially a mixture of various antibodies raised against the same antigen, but which recognize different epitopes, or regions of the antigen." Hurwitz WS at ¶ 15.

[12] Nude mice are mice that have had their immune systems removed, enabling rapid development of a tumor once cancer cells are injected into the mouse's body. See Pirak WS at ¶ 90.

[13] Immortalized cell lines are capable of "indefinitely produc[ing] a pure antibody against an antigen of choice." Lippmann Report at 7.

of choice and can be reproduced indefinitely. See id. The Köhler/Milstein method of creating monoclonal antibodies is discussed further infra.

2. EGF and EGFR

Epidermal growth factor ("EGF") is "a small protein which functions to stimulate the growth and maturation of various organs in the body," including the lungs and kidneys. Lippmann Report at 5. The cells forming these various organs produce and excrete EGF into the body, where it binds to the epidermal growth factor receptors ("EGFR") found on the surfaces of some types of cells. See id. at 6. EGFR is a protein that spans the cell membrane, meaning that it has both an intracellular and an extracellular domain, as well as a portion that actually crosses the cell membrane. When EGF binds to EGFR, the EGFR's structure changes, inducing a series of signals to be sent to the cell nucleus that result in the cell proliferating. See id. at 6. This signaling mechanism is regulated in normal, healthy cells, such that the signaling will cease when the cell has sufficiently proliferated. However, in cancer cells, this mechanism is often damaged, resulting in uncontrolled cell growth. See id.

B. The Named Inventors

Before analyzing the putative contributions of the scientists claiming inventorship, we review their backgrounds

for two purposes: first, to determine the extent to which the subject matter of the '866 patent seems aligned with their prior research; and second, in light of Schlessinger's suggestion that he "knew" the Weizmann scientists' research protocol, we review some of their prior published works in order to evaluate whether Schlessinger could have predicted the course of their experimentation. We begin by reviewing the professional accomplishments and interests of the named inventors.

Dr. Schlessinger received a Bachelors Degree in Chemistry and Physics and a Masters Degree in Chemistry from Hebrew University in Jerusalem. Schlessinger WS at ¶ 2. In 1974, he obtained his Ph.D. from the Weizmann after completing a thesis entitled "Study of Chemical and Biological Systems by Circular Polarization of Fluorescence." Id. at ¶ 3. After several years working at a variety of institutions, including Cornell University and the National Cancer Institute ("NCI") of the United States National Institutes of Health ("NIH"), see id. at ¶¶ 4, 11, Schlessinger returned to the Weizmann in 1978, eventually becoming a professor in the Department of Chemical Immunology. Id. at ¶ 12. Schlessinger's work at the Weizmann focused on EGF and EGFR, and the mechanisms by which EGF signals various cell responses. Id. at 27. Among the honors Schlessinger has received during his career is the Dan David

Prize.[14] Schlessinger has also been elected to, inter alia, the American Academy of Arts and Sciences, the National Academy of Sciences, and the Institute of Medicine of the National Academies. Schlessinger WS at ¶ 22.

In late September 1985, while still employed at the Weizmann, Schlessinger accepted a job offer to serve as a Research Director at Meloy. See Trial Tr. ("Tr.") 572, line 22 to 573, line 4; see also PTX020.[15] By the end of November 1985, Schlessinger's visa permitting him to work at Meloy had been approved, and he had begun working at Meloy. See Tr. 586, line 20 to 587, line 5; see also PTX023. However, Schlessinger did not apply for a sabbatical from the Weizmann until January 1986, and his application was not approved until March 4, 1986. See Tr. 575, lines 3-7. Schlessinger acknowledges that until March 4, 1986, "at least as far as the Weizmann was concerned, [he was] still on the books as a full-time Professor who had not gone on sabbatical . . . ." Tr. 574, line 24 to 575, line 2. Moreover, Schlessinger acknowledges that under his agreement with the Weizmann in place at the time, "there was absolutely no

[14] Somewhat ironically, Schlessinger shared the prize with Dr. John Mendelsohn, who created the antibody that ImClone sells under the name Erbitux. This fact is discussed at greater length infra.

[15] In citing to exhibits introduced at trial by the parties, we use the Bates numbers they provided. "PTX" stands for "Plaintiff's Trial Exhibit," while "DTX" stands for "Defendants' Trial Exhibit." The initials "RPR" following a "DTX" citation stand for "Rhone-Poulenc Rorer."

doubt that if [he] made an invention" during the period from November 1985 through March 4, 1986, "it would belong to the Weizmann." Tr. 576, lines 15-18.

Among Schlessinger's responsibilities as Research Director at Meloy/Rorer was hiring staff. See Schlessinger WS at ¶ 36. As relevant here, Schlessinger initially hired two colleagues from the Weizmann, Drs. Kris and Bellot. See id. Schlessinger subsequently hired Dr. Givol, another Weizmann scientist, who established a separate laboratory within Schlessinger's department at Meloy/Rorer, as did Kris. See id.; see also Givol WS at ¶ 15. Dr. Kris holds a Ph.D. from the University of Florida in immunology/medical microbiology; his thesis involved the role of antibodies in fighting influenza. See Kris WS at ¶ 2. Dr. Givol received his Ph.D. from the Weizmann in 1964, having completed a thesis entitled "Studies of Structure and Activity of Antibodies to Natural and Synthetic Antigens." See Givol WS at ¶ 2. Dr. Bellot earned a Ph.D. from the Université de Provence in 1984 for a thesis about monitoring the cellular proliferation of colon cancer cells. See Bellot WS at ¶¶ 3-4.

After leaving Rorer in 1990, Schlessinger accepted an appointment at New York University, where he subsequently became Chairman of the Department of Pharmacology. See Schlessinger WS at ¶ 14. Subsequently, Schlessinger became Chairman of the Department of Pharmacology at the Yale University School of

Medicine. See id. Since his time at Rorer, Schlessinger has also co-founded two biotechnology companies, SUGEN, Inc. ("SUGEN") and Plexxikon Inc. ("Plexxikon"), both of which are involved in developing anti-cancer drugs. See id. at ¶¶ 15-18.

1. Prior Research of the Named Inventors

According to Scientist magazine, Dr. Schlessinger's publications are among the most-cited papers in the world. See Schlessinger WS at ¶ 20; DTX930. Schlessinger has a long history of researching human cells and, particularly, cell surface receptors. See Schlessinger WS at ¶ 18. In 1978, while at the Weizmann Institute, Schlessinger demonstrated that EGF controls EGFR signaling by what he terms "control receptor dimerization." Schlessinger WS at ¶ 19. Dimerization describes the manner in which two EGF receptors move laterally on the cell surface such that they both attach to the same EGF molecule, initiating the cell signaling process. See id.; see also PTX240 (DVD provided by Dr. Lippmann, demonstrating dimerization). In 1984, Schlessinger and two other scientists, Michael Waterfield and Axel Ullrich, discovered that a virus causing leukemia in chickens contained v-erb-B, a cancer gene. Schlessinger WS at ¶ 20. Moreover, they discovered a "close similarity between epidermal growth factor receptor and the protein sequences encoded by the v-erb-B cancer gene." Id. This discovery was published in Nature, a preeminent scientific journal. See id.

Shortly after this discovery, Schlessinger, along with Kris and others, demonstrated that EGFR is over-expressed in malignant brain tumors. See id. at ¶ 21. This discovery indicated that the EGF-EGFR signaling mechanism might play a role in human cancer. See id.

While conducting his post-doctoral research at the NIH in 1964-65, Givol isolated and characterized an enzyme known as Protein Disulphide Isomerase, which, inter alia, "protects brain cells from misfolded proteins and guards them against Alzheimer's and Parkinson's disease." Givol WS at ¶ 9. Subsequently, while at the Weizmann in 1972-73, Givol and other researchers "discovered the smallest active antibody fragment that retains full binding capacity of the original antibody," which he named the "Fragment variable" ("Fv"). Id. at ¶ 10. Givol's team determined that the Fv is the "variable region of the antibody that differs among antibodies and determines the antigen to which the antibody binds." Id. Moreover, Givol and his team found "that by creating an antibody with only the Fv portion, it was less likely that the body's own immune system would rebel against its introduction into the system." Id. Givol describes the discovery and characterization of the Fv as "one of the most known contributions of the Weizmann Institute to immunology." Id. About ten years after this discovery, in 1982 or 1983, Givol and other scientists at the Weizmann cloned

and sequenced a gene known as "tumor protein 53" ("tp53"). See id. at ¶ 11. Givol and his fellow researchers determined that tp53 "regulates the cell cycle and controls the mechanism for apoptosis (a mechanism of programmed cell death)." Id. The scientists' work with tp53 "paved the way to study the molecular genetics of cancer." Id. Thus, Givol, like Schlessinger, has a long history of research at the molecular level relating to "basic biological problems," see Givol WS at ¶ 12, some of which eventually has proven to have therapeutic applications. See id. at ¶ 11 (describing how tp53 is now being developed for clinical use by biotechnology companies). Givol explains that Schlessinger invited him to come to Meloy/Rorer because he "had experience in researching monoclonal antibodies, and in molecular biology, genetic engineering, DNA sequencing and Fv fragments." Id. at ¶ 15.

Kris worked a great deal with EGFR while he was a post-doctoral fellow in Schlessinger's laboratory, beginning in 1983, in particular working with polyclonal antibodies against the EGF receptor.[16] Specifically, Kris was involved with Schlessinger's research relating to the cell signaling function of the v-erb-B protein, discussed supra. See Kris WS at ¶ 10. In February

[16] Kris explains that he worked with polyclonal antibodies rather than monoclonal antibodies because they are "easier to generate . . . ." See Kris WS at ¶ 9.

1985, Schlessinger, Kris, and others published an article in Biotechnology, a scientific journal, in which they discussed the potential role of the EGF-EGFR signaling mechanism in cancer, observing that "[r]ecent studies indicate that oncogenes are linked to growth factors and to growth factor receptors, suggesting that these molecules participate in the proliferation of normal and neoplastic cells." Kris WS at ¶ 12; DTX915 at 135.

Dr. Bellot joined Schlessinger's laboratory at the Weizmann in 1985 after working at Immunotech, a French company where Bellot "made monoclonal antibodies against various proteins . . . ." Bellot WS at ¶¶ 5, 7. Bellot sought to work with Schlessinger after "learn[ing] of his work with growth factors from the published literature" while preparing her thesis. Id. at ¶ 6. Because Bellot was working at a private company before joining the Weizmann, and very soon thereafter left to join Schlessinger at Meloy/Rorer, she does not have as extensive a list of published research papers as her colleagues, though the record clearly reflects her skill in producing monoclonal antibodies according to the Köhler/Milstein method.

C. The Weizmann Scientists

Professor Sela received his Ph.D. from the Hebrew University in 1954 for research he conducted at the Weizmann's Department of Biophysics. See Sela WS at ¶ 4. Currently, Sela

is the Institute Professor of Immunology at the Weizmann, only the second person to be given the title of Institute Professor.[17] See id. at ¶ 5. From 1975 to 1985, Sela served as the President of the Weizmann, during which time he was elected to be a Foreign Associate of the National Academy of Sciences. See id. at ¶¶ 7, 10. Sela's research throughout his career has focused on therapies for cancer and Multiple Sclerosis ("MS"). See id. at ¶ 14. Sela, along with collaborators, invented Copaxone, a drug that helps prevent relapses and new brain lesion development in about 100,000 American MS patients. See id. at ¶ 15.

Hurwitz retired from the Department of Chemical Immunology at the Weizmann in July 1999. See Hurwitz WS at ¶ 1. Hurwitz began working at the Weizmann in 1963 under Dr. Sela, and earned her Ph.D. from the Weizmann in 1974. See id. at ¶ 4. After spending a year engaged in post-doctoral research at the NIH, Hurwitz returned to the Weizmann, where she continued to work with Sela for the remainder of her career. See id. at ¶¶ 4-5. From 1975 until her retirement, Hurwitz held the title of "Engineer," placing her in charge of certain specialized technical work in Sela's laboratory. See id. at ¶ 5. Her

[17] Ephraim Katzir, a former President of the State of Israel, was the first person to be awarded the title of Institute Professor, an honor conferred upon him by Sela during the ten years he served as President of the Weizmann.

position also enabled her to perform some independent research. See id. at ¶ 6.

Pirak obtained her Ph.D. in biochemistry and cancer sciences in 1984 from the Universite Catholique de Louvain la Neuve in Belgium, where she carried out research for Professor Christian de Dube, a Nobel Prize winner in Medicine and Physiology. See Pirak WS at ¶¶ 5-6. As part of the research for her thesis, Pirak applied the Köhler/Milstein method for creating monoclonal antibodies. See id. at ¶ 19. From 1984 to 1992, Pirak served as a research scientist at the Weizmann. See id. at ¶ 3. She currently serves as Vice President of Technologies at Meytav Technological Incubator Ltd., an Israeli biotechnology company. See id. at ¶ 1.

1. Prior Research of the Weizmann Scientists

Professor Sela has spent most of the past fifty years at the Weizmann, where he has focused a great deal of his research on targeting cancer cells with anti-cancer drugs. See Sela WS at ¶¶ 6, 17-19. In the 1970s, Sela and other scientists at the Weizmann pioneered the "guided missile" approach to cancer therapy, whereby researchers seek to deliver anti-cancer drugs to cancer cells while minimizing harm to noncancerous cells. See id. at ¶ 17. This "guided missile" approach is driven by the fact that anti-cancer drugs are generally toxic both to cancerous and noncancerous cells, causing the harmful side

effects of chemotherapy. See id. at ¶ 18. Sela's laboratory thus sought ways to target cancer cells by conjugating, or chemically attaching, anti-cancer drugs to substances that would seek out and deliver the drugs only to cancer cells. See id. at ¶ 19. Sela's extensive research into the targeting of cancer cells is reflected in the list of published papers attached to his curriculum vitae. See generally PTX169; see especially DTX521, DTX243, PTX172, PTX175.

As mentioned supra, Pirak's thesis involved preparing and purifying monoclonal antibodies. See Pirak WS at ¶ 18. Her specific objective was to bind anti-cancer drugs "through a suitable linkage to specific antibodies [that] are capable of killing selectively breast cancer cells." Id. For her thesis research, Pirak and a colleague prepared conjugates of monoclonal antibodies and daunomycin and doxorubicin.[18] See id. at ¶ 20. Pirak's thesis also discussed using membrane receptors, including EGFR, as sites through which anti-cancer drugs could be delivered to tumor cells. See id. at ¶ 22. Moreover, in order to obtain her Ph.D., Pirak was required to submit a theoretical research project as part of an "annex thesis," which involved giving a lecture in addition to submitting a paper. See id. at ¶ 23. Pirak lectured on

[18] Significantly, Pirak decided to test these same two anti-cancer drugs in the research project at issue in this case.

oncogenes, including ErbB 2, which is structurally related to EGFR. See id. As Pirak explains, "[t]hrough this work, I became even more familiar with the role that EGF and EGF-receptors had in cancer." Id. at ¶ 23. In 1984, shortly after presenting her thesis, Pirak was invited by Sela to join his laboratory at the Weizmann as a Research Fellow. See id. at ¶ 25.

Before retiring in 1999, Hurwitz spent several decades in Sela's laboratory at the Weizmann involved in research in the fields of immunochemistry and immunotherapy; in particular, she worked on a large number of conjugate and targeting studies related to Sela's "guided missile" approach to treating disease. See Hurwitz WS at ¶¶ 4-6, 11-12. Hurwitz explains that she and Sela hypothesized "that antibodies which could either recognize cancer cells specifically or at a higher affinity than normal cells could be used to target anti-cancer drugs directly to such cells. We were therefore looking for an effective combination of an anti-cancer drug with a carrier that would have strong affinity for cancerous cells." Id. at ¶ 14.

In 1975, Hurwitz co-authored a paper with Sela and others entitled "The Specific Cytotoxic Effects of Daunomycin Conjugated to Antitumor Antibodies." See DTX521. This paper described a research project in which Sela's laboratory employed a mixture of polyclonal antibodies and the free drug as a

control to the titular experiment. As discussed infra, it is significant that Sela's laboratory had not yet begun using polymer bridges in creating their conjugates. See id.; see also Hurwitz WS at ¶ 19. Moreover, the mixture tested in this experiment did not exhibit a cytotoxic effect, let alone the synergy[19] that would later be observed in the experiments performed with mAb 108, one of the two monoclonal antibodies Schlessinger provided to the Weizmann scientists. See DTX521; see also Hurwitz WS at ¶ 19. Three years later, Hurwitz, Sela, and others published a paper in the International Journal of Cancer in which a mixture of an anti-cancer drug and a polyclonal antibody was used as a control to an experiment focusing on the use of conjugates that were not bound by polymer bridges. See PTX172. In this case, however, the results from the mixture experiments did indicate a potential therapeutic effect. See Hurwitz WS at ¶ 20; PTX172.

Subsequently, in 1982, Hurwitz and Sela collaborated with scientists from the Hokkaido University School of Medicine (the "Hokkaido") in Japan on research that eventually led to the publication of a paper entitled "Effect of a conjugate of daunomycin and antibodies to rat α-fetoprotein on the growth of

[19] In the context of cancer research, "synergy" occurs when the effect of administering two substances to a tumor cell has a "more than merely additive" effect; i.e., the combined cytotoxic effect exceeds the sum of the cytotoxic effect of each substance administered by itself. Hurwitz WS at ¶ 83.

α-fetoprotein-producing tumor cells." See DTX722. Here, Hurwitz prepared conjugates of polyclonal antibodies at the Weizmann, using a polymer bridge to load daunomycin onto the antibodies. See id.; see also Hurwitz WS at ¶ 21. However, Hurwitz did not participate in the actual in vivo experiments described in the paper, as they were conducted at the Hokkaido. See Hurwitz WS at ¶ 21. This is the only example of a published paper on which Hurwitz was a co-author where a mixture of free drug and antibody was used as a control to an experiment testing a conjugate of drug and antibody bound by a polymer bridge.[20] As

[20] This fact is at odds with the repeated insistence of defendants that Schlessinger knew Hurwitz would perform a mixture experiment, "since such a mixture was tested whether the test focused on conjugates or unconjugated mixtures" in Hurwitz's prior research. Defendant's Post-Trial Brief ("Def. Br.") at 33. In fact, Hurwitz's prior published papers do not reflect a single, fixed protocol, which always involved the same experimental group and the same controls, but rather a wide range of experimental models that use different controls for different research projects. The suggestion that Schlessinger "knew" Hurwitz would test an unconjugated mixture without any direction from him, and when he also knew that she, Sela, and Pirak were focused on conjugate studies cannot be credited.

Moreover, Schlessinger testified that he was "aware of" the papers Hurwitz had published. Tr. 561 line 25. While we do not doubt Schlessinger had a general awareness of the work Hurwitz did while they were colleagues at the Weizmann, we do not credit his suggestion that he had any particular knowledge of her testing protocols, beyond his general awareness that she was involved in the conjugate studies in Sela's laboratory. Significantly, at the time Schlessinger delivered mAbs 96 and 108 to the Weizmann scientists, he had already published approximately 120 peer-reviewed papers, yet had never cited to any paper on which Hurwitz was listed as a co-author. See Tr. 562 line 25 to 563 line 11. In fact, Schlessinger testified that his papers "were on totally different subjects" from Hurwitz's work. Tr. 563 lines 12-13. Finally, Schlessinger testified that he had no specific recollection of reading any of the papers Hurwitz co-authored that he claimed to be "aware of" in his witness statement. See Tr. 563 lines 20 to 23. Thus, we cannot impute to Schlessinger knowledge

noted earlier, Hurwitz did not perform the mixture experiments and the antibodies used were polyclonal, rather than monoclonal. See id.

Hurwitz also published a paper in 1986, entitled "A Synergistic Effect between Anti-Idiotype Antibodies and Anti-neoplastic Drugs in the Therapy of a Murine B-cell Tumor," in collaboration with Professor J. Haimovich ("Haimovich") of Tel Aviv University, where all the research for the paper occurred.[21] See PTX188. Hurwitz and Haimovich tested mixtures of polyclonal antibodies and anti-cancer drugs for this paper; they did not test any conjugates, using the free drug and the free antibody as their two controls. See id.; see also Hurwitz WS at ¶ 22. Hurwitz and Haimovich observed a synergistic effect when the mixture was administered in vivo.[22] See PTX188. This represents the only instance where Hurwitz published a paper

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of all of Hurwitz's relevant prior research at the moment that he provided mAbs 96 and 108 to the Weizmann.

[21] Professor Sela was not involved in this project.

[22] Significantly, despite Schlessinger's testimony that he "knew of" this paper at the time he delivered mAbs 96 and 108 to the Weizmann, discussed infra, Schlessinger was unaware that the research described had taken place at Tel Aviv University. Notably, the paper was published after Schlessinger went on sabbatical from the Weizmann. Schlessinger WS at ¶ 54(v); see also Tr. 565 line 24 to 566 line 13. Schlessinger also testified that while he made "some effort" to keep up with Hurwitz's papers once he went to Meloy/Rorer, that effort was "[n]ot systematic." Tr. 568 line 6. Finally, Schlessinger testified that he did "not remember specific papers" that he may have read once he went to Meloy/Rorer. Tr. 569 line 1. In short, Schlessinger provided no reliable basis for the Court to conclude that he was in fact aware of the paper Hurwitz published in 1986 with Haimovich.

reporting an observed synergistic effect in an experiment involving a mixture of an antibody and an anti-cancer drug.

D. The Creation of Monoclonal Antibodies 96 and 108

In the spring of 1986, Schlessinger, Bellot and Kris, who were by then all working at Meloy, began developing monoclonal antibodies directed against EGFR. See Bellot WS at ¶ 15. Although the actual creation of the relevant antibodies occurred in 1986, the genesis of the project occurred in October 1984, when Schlessinger, who was then still at the Weizmann full-time, applied for a grant from the US-Israel Binational Science Foundation ("BSF") in order to, inter alia, generate antibodies "for structural and functional studies of EGF-receptor and V-erb-B protein." PTX016-002. Under the heading "Objectives and expected significance of the research," Schlessinger stated that "[t]he major objective of the proposed research is to understand the mechanism of epidermal growth factor (EGF) and its membrane receptor in normal growth and in neoplasma." PTX016-014. Schlessinger's proposal continues by noting that he plans to generate antibodies "as a diagnostic tool to explore structure/function relationships in the EGF-receptor and the V-erb-B protein." PTX016-015. Significantly, the grant application does not suggest the use of the antibodies as anything other than a research tool; Schlessinger did not state

that he anticipated using the antibodies for cancer therapy. See PTX016.

The work that was done under the BSF grant began at the Weizmann, though Schlessinger is unclear to what extent the same research was continued at Meloy/Rorer. See Tr. 605 lines 24-25 ("People may have moved back and forth and – but probably – I would guess that most of it was done at the Weizmann."). In any event, pursuant to the BSF grant, Dr. Etta Livneh ("Livneh") created CH-71 cells, which are Chinese Hamster Ovary cells genetically engineered to express the extracellular portion of human EGFR. See Bellot WS at ¶ 17. These CH-71 cells had been created by Livneh at the Weizmann before Schlessinger and his colleagues went to Meloy/Rorer. See, e.g., Tr. 400 lines 4-5.

Bellot testified that by the mid-1980s, when she created the antibodies relevant to this case in Schlessinger's laboratory at Meloy, the Köhler/Milstein process for producing monoclonal antibodies was a "matter of routine . . . for anybody who was working in the field," although the process was still "laborious." Tr. 417 line 12 to 418 line 1. In order to create the monoclonal antibodies pursuant to the Köhler/Milstein process, Bellot began by immunizing mice with the CH-71 cells obtained from the Weizmann. See Bellot WS at ¶ 17. Schlessinger's laboratory "did not get permission to take" the CH-71 cells from the Weizmann, despite the fact that

Schlessinger was on sabbatical from the Weizmann and working at Meloy at the time he procured them. See Tr. 664 line 2.[23]

[23] Schlessinger's explanation for why he believed it was permissible for him to take the CH-71 cells, despite knowing they were the property of the Weizmann, can most generously be described as strained:

> **Q**: The 108 antibody was made with a cell line that you did take from the Weizmann, correct?
> **Schlessinger**: Yes.
> **Q**: And you never got permission to take that?
> **A**: Well - -
> **Q**: Yes or no question. You never got permission to take it, right?
> **A**: I did not get permission to take it.
> **Q**: And you have said you think that it was OK to take that because you think it was in the public domain, right?
> **A**: It was in the public domain.
> **Q**: But you have said on the other hand it was not OK for people to take the 108 antibody because that was not in the public domain, right?
> **A**: It was not in the public domain.
> **Q**: So this is yet another example of where the rules are different depending on what suits your convenience?
> **A**: I don't think so. The cell lines was [sic] in a stage of publication. It was based on materials that I received from Genentech without strings attached. If I were to start have [sic] this exchange for the cell lines, you may find that there is a tremendous record of who gave to what. This was a non - - this was totally public domain information that I have given to many labs, including to my own lab.
> **Q**: Just a second. I don't want to quibble, but look, you told us that Francoise Bellot started work and did the first immunizations in June of 1986, right?
> **A**: Yes.
> **Q**: And the Livneh paper, the first public disclosure of the CH-71 cell line wasn't until August of 1986, right?
> **A**: Yes, but we had - -
> **Q**: You have answered my question.
> **A**: Yes.
> **Q**: So by your own logic, it was not in the public domain when you took it, right?

Bellot used the CH-71 cells taken from the Weizmann for several reasons: first, because Schlessinger desired to study the EGFR signaling mechanism, CH-71 cells were ideal because they expressed the extracellular domain of EGFR as the antigen;[24] second, CH-71 cells express large numbers of EGF receptors on their surface, again making them ideal for developing antibodies against EGFR; and third, CH-71 cells do not contain A-431 carbohydrate chains attached to the extracellular domain, such that the antibodies generated would bind to the protein, rather than the carbohydrate portion, of the EGFR extracellular domain. See Bellot WS at ¶ 17. After Bellot oversaw the immunization of eight mice, four of which were immunized with CH-71 cells and four of which were immunized with CH-71 cell membranes, Bellot

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> **A**: It was in - - I had given it to Axel Ullrich [a scientist with whom Schlessinger has published several papers].
> **Q**: Axel Ullrich is not in the public domain, right?
> **A**: Axel Ullrich is part of the public domain because it's out of my lab.
> **Q**: So we can agree you took something that was developed at the Weizmann Institute, using grant money that had been given to the Weizmann Institute, and you brought it to a commercial company, you used it to develop an antibody for the benefit of the commercial company, and you then took the position that the antibody was proprietary to the commercial company. That's all true, isn't it?
> **A**: Yes.

Tr. 663 line 20 to 665 line 16.

[24] In other words, by using cells that express the extra-cellular domain of EGFR, the resulting antibody likely would bind to EGFR.

performed tests on the sera, i.e., the fluid portion of an animal's blood, of seven of the mice in order to determine whether the sera contained antibodies that bound to EGFR. See id. at ¶ 22.[25] Bellot recorded all of the testing relevant to the instant dispute on loose sheets of paper, which were stored in folders, despite a Meloy company policy of recording all scientific data in signed, dated laboratory notebooks. See, e.g., Tr. 403 line 25 to 406 line 12. Bellot's initial testing revealed that all seven mice whose sera she tested were producing antibodies that bound to EGFR. See Bellot WS at ¶ 23.

After running several additional tests on the sera, Bellot removed spleen cells from two of the mice, labeled 3A and 6A, which were then fused to myeloma cells to make hybridomas, which are immortalized cells with the capacity to proliferate indefinitely. See id. at ¶¶ 18-21, 28; Lippmann Report at 8. This last step occurred on August 23, 1986. See id. at ¶ 21. Cells generated from mixtures of spleen cells, myeloma cells, and hybridoma cells were then diluted in Hypoxanthin-Azaserin selection medium, enabling the hybridoma cells, but not the myeloma cells, to grow (the spleen cells die in the culture)

[25] Bellot also states that she performed tests to determine whether the serum contained antibodies that inhibited the binding of EGF to EGFR. See Bellot WS at ¶ 22. The question of whether Bellot's testing actually determined whether the antibodies she generated inhibited the binding of EGF to EGFR was hotly disputed throughout the trial, and will be discussed in detail infra.

before being placed into twenty-four plates, each containing ninety-six wells. See id. at ¶ 29. Each well was then assigned a number, from 1 through 2304, and was observed for cell growth; those wells exhibiting a high level of growth were then tested for monoclonal antibodies that bound to human EGFR. See id. at ¶¶ 30-31. Eventually, Bellot focused on eleven of the wells indicating the presence of such antibodies. See id. at ¶ 36. All of these test results are found in the loose papers Bellot kept in folders, though she acknowledges that she does not recognize the handwriting on some of the documents.[26] See id. at ¶ 37.

After determining which of the eleven antibodies were the most promising, Bellot proceeded to make sub-clones of the hybridomas that produced mAbs 42, 80, 96, 108, 123, and 224.[27] See id. at ¶¶ 38-39. Subsequently, Bellot asked Meloy technicians in Springfield, Virginia to make ascites[28] for several of the sub-clones, including sub-clones of mAbs 96 and 108. See id. at ¶ 41. Bellot then performed further tests to

[26] Because Bellot did not keep organized notebooks, and in fact could not recognize much of the handwriting in her own folders, the Court was left without a clear picture of what experiments the named inventors performed, and in what order.

[27] These sub-clones were designated by adding ".1, .2, etc." to the end of the number of the relevant antibody. See Bellot WS at ¶ 39.

[28] Ascites fluid is a highly concentrated solution containing antibodies, which is useful to have when one intends to perform a large number of experiments with an antibody. See Bellot WS at ¶ 41.

determine whether the mAbs she had created inhibited the growth of cells that are mitogenically stimulated by EGF.[29] See id. at ¶ 52. Although the handwriting on the relevant documents is not Bellot's, and, as before, the results appear on loose sheets of paper instead of in signed, dated notebooks, see id. at ¶ 54, plaintiff does not apparently dispute that someone in Schlessinger's laboratory at Meloy performed tests during this time period to determine whether certain of the mAbs Bellot generated inhibited cell growth. Importantly, the type of cells Bellot tested were normal, noncancerous human foreskin fibroblast ("HFF") cells, not cancer cells. Tr. 438 lines 2-11. These tests were conducted with HFF cells despite the fact that Bellot's laboratory at Meloy had "many examples of human tumor cells," Tr. 438 line 13, including KB cancer cells, which are mitogenically stimulated by EGF. See, e.g., Pirak WS at ¶ 61.

One test on the HFF cells, dated December 12, 1986, indicates that sub-clones of mAbs 96 and 108 inhibited the growth of these HFF cells, while three of the other mAbs tested did not. See Bellot WS at ¶ 53; DTX933: RPR 10946-47. Again, these documents are not in Bellot's handwriting despite being found in her folder. Significantly, mAb 96 is an IgM antibody,

[29] The phrase "cells that are mitogenically stimulated by EGF" refers to any type of cell that is stimulated to proliferate when EGF attaches to the EGFR located on the surface of that cell. See PTX240. Thus, to "mitogenically stimulate" a cell is to induce it to divide.

meaning that it is a pentameter comprised of five antibody units, and is thus considered to be too large to be used for therapeutic purposes. See Pirak WS at ¶ 74; see also Tr. 549 lines 6-11 (Schlessinger testifying that "I never thought that this antibody [mAb 96] will be a candidate [for cancer therapy] because of its size."). MAb 108, however, is an IgG antibody, which contains only a single Y-shaped structure, rather than five such structures linked together. See Tr. 282 lines 14-18. Schlessinger agrees with the plaintiff that only IgG antibodies are useful in cancer therapy, as IgM antibodies "are too bulky and too large, and they are not easily produced and handled."[30] Tr. 506 lines 19-20.

[30] Schlessinger testified that although he "always thought more about [mAb 96] as a control" for the experiments performed by the Weizmann scientists, Tr. 549 lines 7-8, the Court also heard testimony that it might have been possible to purify mAb 96 by breaking it into five fragments and using one of those fragments for in vivo testing. See, e.g., Tr. 231 line 22 to 232 line 4. It appears that Pirak briefly contemplated doing this, but quickly abandoned the idea. See id.; Pirak WS at ¶ 74.

All of the tests Schlessinger oversaw at Meloy/Rorer were performed in vitro, i.e., in a controlled laboratory setting in cultures. Dr. Alain Schreiber ("Schreiber"), who worked at Meloy/Rorer during the relevant time period, testified that it would have been difficult to perform in vivo tests, i.e., testing on live animals, at Meloy/Rorer because of the "significant financial resources" that would have to be expended to obtain necessary "bureaucratic approvals." Schreiber WS at ¶ 16. Consequently, Schreiber believed that "it was more expedient to have the [in vivo] tests run in laboratories that were continuously using animal experiments for cancer research," such as the Weizmann.[31] Id. at ¶ 16.

1. Additional Characterization of mAbs 96 and 108

One of the issues most hotly disputed among the parties is the extent to which each set of purported inventors had demonstrated that mAb 108 inhibited the binding of EGF to EGFR, which is required by element (iii) of Claim 1 of the patent ("Element (iii)"). The named inventors claim that the experiments conducted by Bellot clearly demonstrate that they had conceived of Element (iii) prior to the research conducted at the Weizmann. Although we need not decide which of the

[31] Schreiber testified that he only became aware that Schlessinger had decided to provide the antibodies to the Weizmann after the fact, and thus his testimony does not relate specifically to the decision to provide mAbs 96 and 108 to the Weizmann scientists. See Schreiber WS at ¶ 15.

purported inventors conceived of this element, for reasons described infra, we nonetheless discuss the arguments presented by both sides as to why the experiments they conducted did or did not demonstrate that mAb 108 inhibits the binding of EGF to EGFR.

Bellot alleges that tests she performed between late 1986 and early 1987 conclusively demonstrate that she appreciated Element (iii). See Bellot WS at ¶ 43. As noted earlier, the documents describing the relevant experiments she performed were kept on loose sheets of paper in three folders. See DTX931; DTX932; DTX933. Some of these documents do suggest that the named inventors appreciated Element (iii), at least in part. For instance, one document contains a chart entitled "Inhibition of I-M-EGF Binding by Monoclonal Antibodies from R. Kris," which appears to show that mAb 108 inhibited between 50% and 57.3% of EGF's capacity to bind to EGFR on the surface of HFF cells and between 40.2% and 44.6% of binding to EGFR expressed by HFL1 cells, another human cell line that expresses EGFR. See DTX933: RPR10948-10949. This document, whose handwriting Bellot did not recognize, see WS at ¶ 22, also suggests that mAbs 96 and 108 inhibit the binding of EGF to EGFR significantly better than the other monoclonal antibodies tested. See id. These results are summarized in another document found in one of Bellot's folders,

dated November 21, 1986, though the handwriting is again not Bellot's.[32] See DTX933: RPR10948; Tr. 457 lines 21-22.

Although these loose documents, along with several others, do suggest that the named inventors might have known that mAb 108 inhibits the binding of EGF to EGFR, there is a significant amount of other evidence suggesting that they failed to appreciate Element (iii). First, all of the Meloy/Rorer scientists' testing was done in vitro on noncancerous cells, whereas Claim 1 refers to cancer cells that are mitogenically stimulated by EGF. Second, as recently as the summary judgment stage of this case, Schlessinger submitted a sworn affidavit stating: "I cannot remember whether we [the named inventors] had also performed tests to confirm our belief that the antibodies [96 and 108] inhibited the binding of EGF to the EGF receptor before I approached Dr. Hurwitz. . . . [O]ne of our early, crude tests showed that mAb 108 did not inhibit the binding of EGF to the EGF receptor."[33] PTX275 at ¶ 18.

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[32] Dr. Kris also testified that the handwriting on this document was not his. See Tr. 827 line 24 to 828 line 5.

[33] On cross-examination, Schlessinger attempted to distance himself from this statement regarding an "early, crude" test:

> **Q**: Sir, that statement that's highlighted up there that says one of your early, crude tests showed monoclonal antibody [sic] did not inhibit the binding of EGF to the EGF receptor, is that statement true?
> **A**: That's true if you want to add here some soluble receptor.

Third, an undated document in Kris' handwriting that was found in one of Bellot's folders states, "Does Ab inhib [sic] EGF effect," beneath which it states "96 – INHIB" and "108 – No effect." DTX198: RPR7255. This document seems to indicate that Kris performed an experiment in which he concluded that while mAb 96 does inhibit the binding of EGF to EGFR, mAb 108 does not. At trial, Kris was uncertain what he meant when he wrote the words "no effect," testifying that it was the "first time" he had seen the piece of paper. See Tr. 831 line 1 to 832 line 1.

Fourth, several papers co-authored by the named inventors suggest that the named inventors had concluded that mAb 108 does not inhibit the binding of EGF to EGFR. A May 1987 draft manuscript entitled "Point Mutation at the ATP Binding Site of EGF-Receptor Abolishes Protein Tyrosine-Kinase Activity and Impairs Normal Receptor Cellular Routing," authored by A.M.

> **Q**: I didn't ask about adding it. I'm asking you whether that statement . . . is true?
> **A**: It's true, it's true when you're talking about soluble receptor.
> **Q**: I'm not asking about soluble receptor. I'm talking about that unqualified statement made by you to this[] court, is it true without explanation?
> **A**: It, unfortunately, is complicated. Really, unfortunately.

Tr. 544 line 25 to 545 line 13. This exchange represents one of many instances in which Schlessinger exhibited great reluctance to acknowledge a fact that he perceived to be injurious to the defendants' case.

Honneger,[34] Schlessinger, Bellot, and others (the "Honneger paper"), states that "IgG-108 . . . does not interfere with the binding of EGF to the receptor (Bellot et al., in preparation)."[35] PTX224-008. Thus, at this point it appears

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[34] A.M. Honneger was a scientist at Meloy/Rorer working in a different laboratory than the named inventors. See Tr. 442 lines 1-6.

[35] Schlessinger explained the statement that 108 does not inhibit EGF binding as follows:

> **Q**: Then it says, antibody 108 does not interfere with the binding of EGF to the receptor. Right?
> **A**: It should have said soluble receptor.
> **Q**: Well, I understand that you now contend it should have said that, but it doesn't say soluble receptor, does it?
> **A**: In the draft of this paper it doesn't say.
> **Q**: And the citation that it gives there is a manuscript by Francoise Bellot. Correct?
> **A**: Yes.
> **Q**: And that manuscript was not directed to soluble receptors, was it?
> **A**: Well, it concluded an experiment probably with soluble receptors.
> **Q**: When you say probably, are you speculating?
> **A**: I have to see it in preparation, so I can't . . . it's difficult to remember all those details.
> **Q**: Fair enough. Now, let's just focus on that statement, on the words that are there. "108 which does not interfere with the binding of EGF to the receptor." Is that statement true or false?
> **A**: It's true for the soluble receptor. It's not true for the receptor on the living intact cells, and I would be delighted to explain it to you if you wish, sir.
> **Q**: What I'm asking is the statement as it appears in those words.
> **A**: Yeah.
> **Q**: Is that statement true or false?
> **A**: It's true for the soluble receptor.

that the named inventors did not believe that mAb 108 inhibited the binding of EGF to its receptor, or at the very least were sufficiently unsure of 108's inhibition effect that they failed to notice what was, in fact, a clear misstatement of its

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> **Q**: But it doesn't say soluble receptor. Is it a true statement that antibody 108 does not interfere with the binding of EGF to the receptor?
> **A**: Well, look, this is more complicated than playing sort of games with words. I'm telling you, I'd be delighted to explain to you this and related studies to all the nature of these interactions. I'd be delighted. If you wish, I'll do that.
> **Q**: Would you agree with me that to the extent that that statement says . . . that 108 does not interfere with the binding of EGF to the receptor on intact cells, it would be a false statement?
> **A**: In – it's true for – it's true for the soluble receptor. It's not true for the intact receptor. So if you want to be specific, you have to describe both of them. And, I'm sorry, there are certain things which are complicated which I'll have to explain. I'll be delighted to do that.
> **The Court**: The only question is: As written, just the language, is it true or not? Without any explanation; as written, is it true or not?
> **A**: Sometimes, sentence —
> **The Court**: That's a yes or no.
> **A**: Well, you know, I – I'm afraid that I cannot categorically say that because —
> **The Court**: You know, it was written by a scientist. It wasn't written by a lawyer. So, as written, without further explanation, is it misleading?
> **A**: It's potentially misleading, yes. That's – that's — yeah, because it doesn't contain the entire story . . . . I fully agree with you that it's misleading.

Tr. 531 line 20 to 534 line 6.

properties. Subsequently, Irit Lax,[36] Schlessinger, Bellot, Givol, and others prepared a manuscript entitled "Domain deletion in the extracellular portion of the EGF-Receptor reduces ligand binding and impairs cell surface expression" (the "Lax paper"), which was submitted for internal review at Rorer on October 1, 1987, long after the Weizmann scientists began their research with mAb 108. See PTX059. This paper states, "mAb 108 . . . does not interfere with the binding of EGF to the receptor and mAb-96 . . . blocks the binding of EGF to the receptor (Bellot et al., in preparation)." PTX059-008. Here, the named inventors co-authored a manuscript in which they appear to hold the belief that while mAb 96 does inhibit the binding of EGF to EGFR, mAb 108 does not. All witnesses now agree that both mAb 96 and mAb 108 do in fact inhibit binding of EGF to EGFR.[37] Notably, there is no document produced by the named inventors during this same time period where they

[36] Irit Lax is another scientist who worked at Meloy/Rorer during the relevant period, in the same laboratory as Dr. Honneger. See, Tr. 442 lines 3-6.

[37] The named inventors testified that it is important to distinguish two types of binding: high-affinity and low-affinity. Specifically, they contend that their repeated statements that mAb 108 does not inhibit the binding of EGF to EGFR referred only to the low-affinity binding, as mAb 108 only inhibits high-affinity binding. See, e.g., Tr. 517 lines 18-20. Although the Court credits this proposition as scientific fact, it remains the case that the named inventors repeatedly suggested in 1986 and 1987 that mAb 108 does not inhibit any kind of binding and have not offered into evidence any sort of contemporaneous qualifying statement explaining that they only meant to refer to low-affinity binding.

unequivocally state that mAb 108 does inhibit the binding of EGF to EGFR.

Thus, at the time of the meeting described in Section F, infra, Schlessinger and the members of his laboratory at Meloy/Rorer were aware that mAbs 96 and 108 bound to the protein portion of the extracellular domain of EGFR, inhibited the growth of HFF cells, and that 96 was an IgM antibody, while 108 was an IgG antibody. However, the record does not support the conclusion that they had fully characterized mAb 108's ability to inhibit the binding of EGF to EGFR; rather, they appeared to be confused about the existence of this property.

E. The Weizmann/Yeda Research Project

In early 1986, Sela and Pirak submitted a grant proposal to the Yeda-Fund, an organization affiliated with the Weizmann that subsidizes applied scientific research, i.e., research that might lead to commercially useful products.[38] See Pirak WS at ¶ 38. The proposal suggested that EGF could be used as a carrier for anti-cancer drugs by conjugating, or chemically attaching, EGF to known drugs. See PTX029. Sela and Pirak also proposed conjugating anti-cancer drugs to monoclonal antibodies that bind to the EGF receptor in order to compare the effectiveness of EGF

[38] Hurwitz offered input on the proposal, but her name does not appear on the document, as it is customary to only list the supervisor (Sela) and the post-doctoral researcher (Pirak) on such grant applications. See Pirak WS at ¶ 39.

and monoclonal antibodies as carriers. See id. As explained in the proposal, "[t]he purpose of the study proposed here is to prepare several conjugates of small anti-neoplastic drugs,[39] directly or via bridges, to EGF on one hand, and to monoclonal antibodies against epidermal growth factor receptor on the other, and to compare their efficiencies on EGF receptor-rich tumors in vitro and, ultimately, in vivo." PTX029-003 to 004. Thus, the Weizmann scientists initially contemplated chemically attaching anti-cancer drugs to EGF and to monoclonal antibodies in order to determine their relative effectiveness in destroying cancer cells possessing a large number of EGF receptors on their surface.[40]

On April 4, 1986, the Yeda-Fund approved the grant proposal, awarding the Weizmann scientists $18,000 to begin their research, and requesting a progress report in six months. See PTX033. The Weizmann scientists immediately began working, with Pirak supervising the day-to-day activities of the laboratory in close collaboration with Hurwitz, while Pirak and

[39] The term "anti-neoplastic" is used synonymously in this Opinion and Order with "anti-cancer" and "chemotherapy."

[40] This grant proposal also states that Professor Schlessinger and his co-workers "will be collaborating with us on the proposed research." PTX029-002. As discussed in detail infra, however, no such collaboration occurred outside of Schlessinger's providing the monoclonal antibodies that Sela's laboratory at the Weizmann used in its research.

Sela met monthly to discuss the results of the research. See Pirak WS at ¶¶ 53-54.

Pirak submitted the first progress report to the Yeda-Fund in October 1986. See PTX041; Pirak WS at ¶ 55. In this report, Pirak explained that EGF was proving to be an unsuitable carrier for anti-cancer drugs, as its low molecular weight made it difficult to load sufficient amounts of the drug to each EGF molecule, which, in turn, inhibited her ability to deliver adequate amounts of the drug to the targeted cells. See PTX041. Significantly, the report reflects that the Weizmann scientists decided to run their tests on KB cancer cells, a type of cancer cell that has a large number of EGF receptors on its surface and is mitogenically stimulated by EGF. See id; see also Pirak WS at ¶¶ 60-63 (explaining Pirak's early decision to switch from using two other types of cancer cells, namely NIH-3T3 and A431 cells, to using KB cells). At the end of the progress report, Pirak states that, "[i]t seems to us that in parallel one should try antibodies against the EGF receptor as carriers for the targeting of drugs to tumor cells rich in exposed EGF receptors." PTX041-004.

At the time that the Weizmann scientists decided to refocus their project on monoclonal antibodies that bound to EGFR, they did not have any such monoclonals readily available in their laboratory. See Pirak WS at ¶ 65. Pirak, having already

created monoclonal antibodies for her thesis work, knew that it would significantly delay the project to create new antibodies. See id. Consequently, Pirak and Hurwitz discussed obtaining monoclonal antibodies against the EGF receptor from, among other sources, Schlessinger, their colleague from the Weizmann, who by then had begun working at Meloy/Rorer. See id.

F. Schlessinger and Hurwitz Meet at the Weizmann

While Schlessinger was employed at Meloy/Rorer, he made periodic visits to the Weizmann; as relevant here, one of those visits occurred between December 30, 1986 and January 8, 1987. See Tr. 589 line 20 to 590 line 16; see also PTX154 (Israeli records indicating the dates Schlessinger entered and left the country). At some point during those ten days, Schlessinger spoke with Hurwitz at the Weizmann.[41] During that brief conversation, Schlessinger told Hurwitz that he had "good" monoclonal antibodies to give her, and offered her mAbs 96 and 108.[42] See Hurwitz WS at ¶ 58; Schlessinger WS at ¶ 59. Though

[41] Schlessinger recalls the conversation occurring outdoors, while Hurwitz recalls it occurring indoors. See Schlessinger WS at ¶ 59; Hurwitz WS at ¶ 57. The parties also dispute who began the conversation. Regardless, neither party disputes that a conversation took place at the Weizmann during this time period. Moreover, it is clear from the record that neither specifically sought the other out on that particular day.

[42] Schlessinger also provided samples of mAbs 96 and 108 to several other laboratories, including laboratories at George Washington University and the Salk Institute. See Schlessinger WS at ¶¶ 51-52. The fact that Schlessinger gave these antibodies to several laboratories undermines his argument that he had conceived of the

the parties disagree about what the term "good" encompassed, at the very least, Hurwitz believed Schlessinger intended "good" to mean monoclonal antibodies that were specific to human EGFR. This understanding was based only on what Hurwitz knew of Schlessinger's work with EGF and EGFR, not upon any specific description Schlessinger offered of the antibodies' properties. See Hurwitz WS at ¶¶ 59-61.[43]

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subject matter of the '866 patent before delivering the antibodies to the Weizmann scientists. Rather, it would suggest that he only generally believed that the antibodies might prove useful, yet did not know quite how or in what context. This conclusion is reinforced by the fact that each of the labs to which he gave mAbs 96 and 108 were engaged in a different type of research. See Tr. 671 lines 11-21 ("Different labs were doing different things.").

[43] Schlessinger provided an account of this conversation containing a great deal more detail than the one provided by Hurwitz. Schlessinger states that he "informed [Hurwitz] that the antibodies were proprietary to Rorer, all commercial rights belonged to Rorer, Rorer's patent department would have to review all publications before they were submitted, and the antibodies could not be given to others without permission." Schlessinger WS at ¶ 59. Schlessinger also claims that he "proposed the possibility to Dr. Hurwitz of testing monoclonal antibody in combination with an anti-neoplastic agent." Id. at ¶ 58. Finally, Schlessinger contends that his understanding of the word "good" in the phrase "good monoclonal antibodies" encompassed all of the attributes of those antibodies that eventually were described in the '866 patent.

We find Schlessinger's account of this conversation not credible for several reasons. First, nearly twenty years have passed since the conversation occurred, such that we doubt Schlessinger remembers its details, especially considering the contorted testimony Schlessinger offered on cross-examination, in which he seemingly attempted to "remember" those details that would bolster defendants' case:

> **Q**: Now, sir, I'd like to find out what precisely was said in your conversation with Dr. Hurwitz. What did you say to her with reference to the 108 antibody?
> **Schlessinger**: I told her that – you know, she was working for quite awhile on different area [sic]

> antibodies we gave her, and these antibodies were no good, for the purpose of joint interest. So I told her we have now very nice antibody, a good antibody, which has properties which would be proper for you to try and set up this – the system that you're using, and that is trying how to see this — whether these antibody are effective in treating tumor cells in mice, conjugated or in mixtures, and you have – and normally what you do is when you have conjugate, you will have to have an antibody which is not conjugated.
> **The Court**: Focus just on exactly what you said to her . . . . [W]hat did you say?
> **A**: Okay. So I told her that we have very good antibodies, and these antibodies could be tested in the scheme that we had discussed in the previous experiments that you have been doing, and in the checking all the different combinations that – of antibodies, drug alone and mixture.

Tr. 592 line 12 to 593 line 7. In effect, Schlessinger's testimony suggested that he recalled precisely instructing Hurwitz on how she should test the antibodies. However, in his witness statement, Schlessinger states that he "did not discuss" the proposed testing protocol with Hurwitz "with great specificity." Schlessinger WS at ¶ 58. Moreover, on cross-examination, Schlessinger admitted both that he could not recall whether the conversation occurred inside or outside, see Tr. 598 lines 1-5, or even whether a third person, Dr. Bilha Schechter, also took part in the conversation. See Tr. 597 lines 13-20.

Second, Schlessinger testified that he anticipated that Hurwitz would use the antibodies in her "system," which he claimed necessarily would entail testing an anti-cancer drug in a mixture with the monoclonal antibodies, whereby the drug and antibody are not chemically attached, as a control to the conjugates of antibody and drug. See Tr. 592 line 20. This testimony is not credible. Most significantly, Schlessinger testified that he had no specific recollection of reading any particular paper written by Hurwitz during that time period. See Tr. 568 line 12 to 569 line 2. Moreover, Schlessinger suggested that while Hurwitz might "tell me about her work," see Tr. 568 line 9, he never testified to having any specific basis to conclude that, by virtue of the simple fact that he provided her antibodies for testing, she would perform a mixture experiment, administering one of the two antibodies Schlessinger provided with any particular anti-cancer drug. In fact, a review of Hurwitz's published papers suggests, as noted earlier, that although she often did use a mixture as a control in her experiments, that mixture usually

consisted of administering the antibody along with the drug Dextran, which Hurwitz frequently used as a "bridge" to load a drug onto the carrier. See, e.g., Tr. 596 lines 11-23. However, as discussed supra, on only one occasion did Hurwitz test the chosen carrier in a mixture with the drug as a control, and in that instance, Hurwitz was not personally involved in the in vivo experiments. Consequently, absent a specific suggestion to test a mixture of antibody and drug, Schlessinger had no reasonable basis to conclude that such an experiment would be performed.

Third, it is implausible that if Schlessinger considered it important at the time that his antibodies be tested in mixtures with anti-cancer drugs, he would have relied on the hope that Hurwitz would perform such an experiment as a control, rather than simply requesting that she test a mixture. Here, Schlessinger knew Sela's laboratory primarily tested conjugates, see Tr. 594 line 4, such that if he desired for a mixture experiment to be performed, he could have simply asked Hurwitz to perform such an experiment, which we are not convinced he ever did.

Fourth, the fact that Schlessinger gave Hurwitz mAb 96, an IgM antibody, is at odds with his suggestion that he knew the outlines of the testing procedures employed at Sela's laboratory, as Schlessinger agreed that only IgG antibodies are useful in cancer therapy, as IgM antibodies "are too bulky and too large, and they are not easily produced and handled." Tr. 506 lines 19-20. Pirak testified that she found it "quite puzzling" that Schlessinger provided mAb 96, Tr. 284 line 17., explaining that she and Hurwitz "abandoned [mAb 96] very quickly and we wondered why [Schlessinger] gave it to us because he knew it was not good. I don't know. I suppose he was supposed to know that it's not good for our purposes." Tr. 231 line 23 to 232 line 1.

Fifth, at his deposition, Schlessinger specifically defined the word "good" in the context of describing mAb 108 as meaning that "[i]t can isolate EGF receptor in a total cell mixture extremely efficiently." Schlessinger Dep. Tr. 251 lines 17-18. At trial, however, he argued that the word "good" also meant that 108 inhibits the binding of EGF to EGFR and that it inhibits the growth of cells that are mitogenically stimulated by EGF. Regardless, in the absence of any generally understood meaning of the adjective "good" when used by scientists to describe antibodies, we cannot impute any knowledge of these antibodies' properties that was in Schlessinger's head at that time to the Weizmann scientists when they began their work with the antibodies.

Sixth, Schlessinger was required by Meloy/Rorer to submit performance objectives, the success of which were evaluated in his annual review report. However, Schlessinger's performance objectives for 1986 and 1987 altogether fail to suggest that he intended to test

Schreiber testified that the in vivo testing eventually performed by Sela's laboratory at the Weizmann was "no different than what a contract research house would do." Id. at ¶ 17. An obvious difference, however, is that there is no creditable evidence that any contract was formed between Meloy/Rorer and Weizmann as to the use of the antibodies given to Sela's

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the antibodies generated at his laboratory in combination with cancer drugs. See PTX046; PTX065. Although both sets of objectives included detailed goals relating to investigating the structure and function of EGF and EGFR, both are silent on the issue of any potential therapeutic purposes for the monoclonal antibodies generated at his laboratory. Considering that Schlessinger's contract provided for additional compensation based on how well he met his stated goals, we do not credit the suggestion that he would have failed to list as an objective his desire to pursue combination studies with anti-cancer drugs if he had in fact specifically contemplated such an idea.

Seventh, we do not believe that the Weizmann scientists would have agreed to the terms Schlessinger suggests he related to Hurwitz. Schlessinger testified that during this meeting with Hurwitz, he "informed her that the antibodies were proprietary to Rorer, all commercial rights belonged to Rorer, Rorer's patent department would have to review all publications before they were submitted, and the antibodies could not be given to others without permission." Schlessinger WS at ¶ 59. In contrast, Hurwitz alleges that Schlessinger "did not impose any limitations on the use of mAb 108," an allegation much more consistent with the other evidence presented to the Court. Hurwitz WS at ¶ 65. Moreover, we credit Hurwitz's testimony that "Professor Sela's laboratory never acted as a service laboratory for other scientists." Hurwitz WS at ¶ 68. Quite simply, the suggestion that Hurwitz would have accepted the antibodies on behalf of the Weizmann if she believed that Schlessinger owned the rights to all of the subsequent research performed in Sela's laboratory is incredible.

Eighth, and perhaps most importantly, despite providing the Court with hundreds of exhibits, defendants have failed to present a single piece of physical or documentary evidence suggesting that Schlessinger or any of the other named inventors contemplated that any particular type of testing would be conducted with mAbs 96 and 108 at Sela's laboratory or had any particular notion about the best way to discover if mAbs 96 or 108 had any practical usefulness.

laboratory. See Tr. 882 lines 1-11 (Schreiber: "I cannot point or I did not find documents" substantiating the allegation in his witness statement that Schlessinger simply outsourced the in vivo testing of mAbs 96 and 108 to Sela's laboratory at the Weizmann). If such a contract did exist, it also would necessarily spell out what type of experiments the Weizmann scientists were obligated to perform, making it clear whether the named inventors anticipated the mixture experiment. Moreover, Schreiber testified that he "was surprised that [the lawyers] could not find a material transfer agreement because it was standard procedure" at Meloy/Rorer to issue "written material transfer agreements for all our proprietary reagents." Tr. 908 lines 2-4; lines 17-18. In fact, Rorer entered into a written transfer agreement with another scientist, Dr. John Mendelsohn, regarding his use of mAb 108. See PTX083. The fact that Meloy/Rorer had a clear policy of requiring that their scientists sign agreements outlining the rights of the parties involved in the transfer of proprietary materials, and entered into such an agreement with a non-Weizmann scientist regarding the very same antibody at issue in this case, bolsters our conclusion that no such agreement existed and that Schlessinger did not place any restrictions on the Weizmann's use of the antibodies his Meloy/Rorer laboratory generated. Additionally, a sample material transfer agreement admitted into evidence

makes clear that it was Rorer's practice to compensate organizations with which it entered into such agreements. See PTX063. Here, however, Rorer did not pay the Weizmann for carrying out more than a year's worth of in vivo experiments. In short, beyond Schlessinger's recollection of telling Hurwitz twenty years ago that Meloy/Rorer retained all of the intellectual property rights to any discoveries the Weizmann scientists might make, there is absolutely no evidence that the named inventors and the Weizmann scientists entered into any such agreement.

In any event, after speaking with Schlessinger, Hurwitz told Pirak about this brief conversation, and Pirak obtained samples of mAbs 96 and 108 from Livneh, then a post-doctoral fellow in Schlessinger's laboratory at the Weizmann. Tr. 598 lines 15-23. Significantly, Schlessinger testified that he provided the antibodies to Livneh to be used as a "research tool," Tr. 599 line 9, not for any potential therapeutic purpose. When Livneh gave the samples to Pirak, Livneh informed Pirak that mAb 96 was an IgM antibody while 108 was an IgG. See Pirak WS at ¶ 69; Tr. 240 lines 18-20. Pirak also knew, apparently from her conversation with Hurwitz, that the antibodies bound to human EGFR.[44] See Pirak WS at ¶¶ 66, 69.

[44] Professor Sela also testified that he recalled having a conversation with Schlessinger about an antibody Schlessinger had

G. Initial Research and Characterization of mAbs 96 and 108

After Hurwitz informed Pirak that they would be able to obtain monoclonal antibodies from Schlessinger, Hurwitz and Pirak met with Sela to formulate an experimental model whereby the antibodies would be conjugated to certain anti-cancer drugs in order to carry the drugs to tumor cells. See Pirak WS at ¶ 70. At the same time, during January of 1987, Sela and Pirak submitted a second grant proposal to the Yeda-Fund, in which they sought funding to continue their research, but with a new emphasis on the "[u]se of monoclonal antibodies directed against the external region of EGF receptor as carriers to antineoplastic drugs for affinity therapy of cancer." PTX045. The Yeda-Fund eventually approved an additional $25,000 of funding on May 10, 1987. See PTX051.

Immediately after submitting the funding request in January 1987, Pirak began performing tests to characterize mAbs 96 and 108. See Pirak ¶¶ 72-73. At this time, Pirak knew very little about their properties, beyond her assumption that both

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created, though Sela does not remember any specifics of this conversation. See Sela WS at ¶ 35. Because Sela indicates Schlessinger never suggested a research protocol and because there was no testimony indicating that Sela used any information he may have learned from Schlessinger during the conversation to guide the research at the Weizmann, the existence and content of this conversation are not important to our analysis. Moreover, if Schlessinger had told Sela during this conversation that the intellectual property rights in any discoveries Sela might make would belong to Meloy/Rorer, we do not believe Sela would have agreed to use Schlessinger's antibodies.

antibodies would bind to EGFR. See id. at ¶ 73. Thus, before beginning any work on conjugates of the antibodies with anti-cancer drugs, Pirak set out to determine their properties. See id. As mentioned earlier, Pirak quickly decided only to focus on mAb 108, as mAb 96 was unsuitable for the proposed research due to its size. See Pirak WS at ¶ 74. Pirak then purified mAb 108 and began analyzing its binding characteristics. See id. at ¶ 73.

Hurwitz and Pirak purified the antibody by "centrifugation, precipitation and chromatography." Pirak WS at ¶ 75. They then prepared and purified certain fragments of the antibody, known as Fab' and $F(ab')_2$ fragments, which are still able to recognize and bind to the same antigen that the entire antibody does.[45] See id. They next evaluated the purity of both mAb 108 and the fragments by a process known as gel electrophoresis. See id. at ¶ 76; see also PTX006 (discussing protocol Pirak, Sela, and Hurwitz employed to evaluate purity).

Before proceeding to the conjugate experiments, the Weizmann scientists also characterized the KB cancer cells with which they had decided to work. See Pirak WS at ¶ 77. Pirak performed several tests, including a cell sorter analysis to

[45] Pirak explains that this step is taken because "[i]n drug targeting, the accessibility of the antibody into the tumor tissue is an issue and therefore fragments are tested in the hope that they will work equally well and more easily access the tumor cells." Pirak WS at ¶ 75.

determine the binding characteristics of mAb 108 and its fragments to the EGF receptors expressed on the surface of the KB cells. See id. at ¶ 80. Moreover, Pirak performed tests to determine where exactly mAb 108 bound to the EGF receptor, which she did by performing a test known as a competitive radioimmunoassay. See Pirak WS at ¶¶ 81-82; see also PTX006 (the 1988 paper) at 1606-07. This radioimmunoassay determined how EGF and mAb 108 competed to bind to the EGF receptors on the KB cells. See Pirak WS at ¶ 82. The results of this radioimmunoassay are reflected in Figure 1(B) of the 1988 paper. See PTX006, Fig. 1(B). Through these preliminary experiments, the Weizmann scientists learned that mAb 108 bound to the extracellular domain of the human EGF receptor and that EGF inhibited the binding of mAb 108 to EGFR. See Pirak WS at ¶ 84.

Pirak testified that these preliminary experiments also revealed, to a "scientific certainty," that not only does EGF inhibit the binding of mAb 108 to EGFR, but also that 108 inhibits the binding of EGF to EGFR, as required by Element (iii). See Tr. 292 lines 20-23. Figure 3 of the 1988 paper reflects a test Pirak ran in order to "analyze[] the effect of EGF and mAb 108 on the growth of KB cells." Pirak WS at ¶ 86. Pirak asserts that Figures 1(B) and Figure 3 from the 1988 paper together disclose Element (iii). Specifically, she testified that these two figures demonstrate that "mAb 108 inhibited the

effect of EGF on the KB cells in vitro and they were no longer stimulated to divide." Pirak WS at ¶ 87. The lower of the two lines of Figure 3, reproduced below, reveals that the number and size of KB colonies decreased in the presence of mAb 108.

Defendants claim that Figures 1(B) and 3 did not enable Pirak to conclude with certainty that mAb 108 inhibits the binding of EGF to EGFR. They point to Pirak's deposition testimony, where she testified that she did not remember if she determined whether 108 inhibited the binding of EGF to EGFR. See Pirak Dep. Tr. at 55 lines 13-16. Moreover, Hurwitz testified that the 1988 paper does not say "clear and cut" that 108 inhibits such binding, although she believes that based on the data in the paper, 108 "would probably inhibit to some extent the binding of the EGF . . . ." Tr. 986 lines 14-16.

Moreover, defendants cite the testimony of plaintiff's expert witness, Dr. Lippmann, who stated that he "believe[s] that Figure 1(B) and the text of the article discussing Figure 3 strongly show that mAb 108 exerts its growth inhibitory effect by perturbing the binding of EGF to EGFR . . . ," but apparently did not conclude this with the same degree of certainty as did Pirak.[46] Defendants' expert, Dr. Aaronson, testified that he does not "believe that any of the tests described in the 1988 article show that mAb 108 inhibits binding of EGF to the EGF receptor." Aaronson WS at ¶ 40. In short, the proper interpretation of the Weizmann scientists' data is debatable. As discussed below, however, we need not decide which side presents the better argument on this issue, as we conclude that defendants are judicially estopped from asserting that the 1988 paper does not disclose Element (iii). See discussion at pp. 120 to 123.

Subsequently, Pirak analyzed the effect of EGF and mAb 108 on KB cells, as illustrated by Figure 3 of the 1988 paper. See Pirak WS at ¶ 86; PTX006, Fig. 3. The results of these experiments revealed that KB cells are mitogenically stimulated by EGF — that is, as EGF is added to colonies of KB cells, the

[46] We note, however, that defense counsel did not ask Lippmann a precise question to determine whether he could conclude with certainty, based only on the information contained in the 1988 paper, whether mAb 108 inhibits the binding of EGF to EGFR.

number of colonies increases. See Pirak WS at ¶ 87; PTX006, Fig. 3. Moreover, Pirak discovered that adding mAb 108 to these colonies inhibited EGF's effect on KB cells, meaning the KB cells stopped dividing and, in fact, the number and size of KB cell colonies decreased once mAb 108 was added. See Pirak WS at ¶ 88; PTX006, Fig. 3. Having observed these promising results, indicating that mAb 108 has an inhibitory effect on the growth of KB cancer cells in vitro, Pirak began in vivo studies with mAb 108.[47] See Pirak WS at ¶¶ 88-89.

For her initial in vivo experiments, Pirak used nude mice, which she injected with KB cells. See Pirak WS at ¶ 90. Once tumors developed, Pirak first determined whether mAb 108 localized to the tumors — that is, she determined whether the antibodies targeted the tumors, rather than other tissues, such that they could potentially be useful as a carrier for anti-cancer drugs. See id. The results of these tests, as memorialized in the 1988 paper, indicate that mAb 108 does in fact localize to the tumor cells. See id. at ¶ 93; PTX006 at

[47] Pirak emphasized in her testimony, as did several other witnesses, that "[i]t is impossible to predict the results of in vivo studies based on preliminary in vitro data." Pirak WS at ¶ 89. As a corollary, she adds, "[a]lthough promising results achieved in vitro may suggest to conduct [sic] similar experiments in animals, there are simply too many variables and it is impossible to predict whether similar phenomenon would be observed in vivo." Id. Similarly, Schlessinger testified that, "you can't really make prediction about science without testing it [sic]." Tr. 527 lines 13-14. The issue of the predictive value of experiments performed in vitro on experiments performed in vivo will be addressed in the discussion section, infra.

1608, col. 2, line 23 to 1609, col. 1, line 2. The interim progress report submitted to the Yeda-Fund in March of 1987 (the "March 1987 report") similarly reveals this promising initial result. See PTX047.

At this point, the Weizmann scientists determined that they were ready to begin testing conjugates of mAb 108 and anti-cancer drugs.[48] See Pirak WS at ¶ 94. They began by conjugating mAb 108 with the drug daunomycin, using a dextran bridge[49] to link the antibody to the drug. See id. at ¶ 95; PTX047. Next, they performed in vitro experiments to test for binding and cytoxicity.[50] See PTX047, Fig. 2. This in vitro testing revealed that the conjugate killed 90% of KB cells at concentrations where daunomycin alone had no effect. See id., Fig. 3; Pirak WS at ¶ 95. Due to these promising in vitro results, the Weizmann scientists proceeded to perform in vivo testing of the 108-daunomycin conjugate. See Pirak WS at ¶ 96.

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[48] Pirak testified that this was the first time that any scientists "had investigated the effect of applying a combination of monoclonal antibodies to EGF receptors with anti-neoplastic agents to any tumor cell line (whether mitogenically stimulated or not). Due to the uncertainties in this sort of research, we had no idea what results we were going to obtain." Pirak WS at ¶ 94. At trial, defendants presented no evidence to refute this testimony.

[49] Hurwitz testified that by the late 1970s-early 1980s, the Weizmann scientists began using polymer bridges, such as dextran, in their conjugate experiments in order to load more drug onto an antibody. See Hurwitz WS at ¶ 23. Hurwitz further explained that using such a bridge "made the binding [between drug and antibody] more predictable and enabled binding of more drug molecules to the antibody without affecting its antigen-binding activity." Id. at ¶ 24.

[50] Cytoxicity describes a substance's ability to kill cells.

The March 1987 report describes the testing protocol for the in vivo experiments on nude mice devised by the Weizmann scientists. See PTX047. Along with the drug-dextran-108 conjugates, they conducted tests of four controls in order to compare the relative therapeutic benefits of the conjugate: (1) the antibody alone; (2) daunomycin alone; (3) daunomycin bound to dextran, without the antibody; and (4) an unconjugated mixture of the drug bound to dextran and the antibody. See id.; Pirak WS at ¶ 97. Significantly, the initial testing protocol did not include a mixture of the free drug (i.e., the drug not bound to dextran) and mAb 108, the mixture that would form the basis for the '866 patent.

The 1988 paper describes the results of these experiments. See PTX006. The Weizmann scientists learned that mAb 108 by itself inhibits the growth of cancer cells in vivo. See PTX006 at 1607, col. 1, lines 35-44. Having discovered that mAb 108 alone might be effective in cancer therapy, the Weizmann scientists engaged in further testing with mAb 108 by, inter alia, investigating the survival rates of nude mice with KB cell tumors after being treated with mAb 108. See Pirak WS at ¶¶ 100-102; PTX006 at 1607 col. 1, line 52 to col.2, line 2, 1609, col. 2, lines 5-6, 8-14, and Fig. 7. The results of these tests indicated that not only did mice treated with mAb 108 survive

longer, but 30% of the mice did not develop tumors at all. See PTX006 at 1609, col. 2, lines 9-12.

Pirak prepared an abstract of the research the Weizmann scientists had performed with mAb 108 for the annual meeting of the Israel Immunological Society, held on May 26, 1987. See PTX192; Pirak WS at ¶ 106. Besides herself, Sela, and Hurwitz, Pirak listed Schlessinger and Bellot as authors, as they had provided the Weizmann scientists with the antibody. See PTX192; Pirak WS at ¶ 106. This short abstract mentions some of the findings the Weizmann scientists had made, but does not mention the cytotoxic properties they had discovered after mAb 108 was administered by itself to nude mice injected with KB cells. See PTX192.

Subsequently, during the summer of 1987, Pirak drafted an abstract revealing the Weizmann scientists' discovery that mAb 108 might have therapeutic value per se, which Pirak intended to present at the UCLA Symposia on Molecular & Cellular Biology, to be held in January of 1988. See Pirak WS at ¶ 107; PTX194. This abstract also listed Schlessinger and Bellot as authors, in addition to the Weizmann scientists. After preparing the draft abstract, Pirak sent a copy to Schlessinger for his review; he received a copy by October 1, 1987, as evidenced by an inter-office memorandum at Rorer referencing the document. See PTX058. Pirak had no discussions whatsoever with Schlessinger

about the results described in the draft abstract until after he received it. See Pirak WS at ¶ 109. Moreover, there is no evidence that Schlessinger inquired about the work being done by the Weizmann scientists or otherwise suggested any particular testing protocols subsequent to his making mAbs 96 and 108 available to Hurwitz and her colleagues. See id; Hurwitz WS at ¶¶ 67-68, 84-85; Sela WS at 35.

In July 1987, Hurwitz left the Weizmann for a sabbatical in Paris, while Pirak continued the research they had been doing with Sela's guidance. See Pirak WS at ¶ 110; Hurwitz WS at ¶ 72. When Hurwitz returned from her sabbatical in late December 1987, she reviewed the research Pirak had conducted in her absence. See Hurwitz ¶¶ 73-74. Pirak and Hurwitz discussed the fact that while the drug-dextran-108 conjugates were somewhat effective in fighting the KB cell tumors, they did not eliminate the tumors altogether. See Hurwitz WS at ¶ 74; Pirak WS at ¶ 111. Hurwitz thus proposed an experiment whereby they would test two cancer drugs, doxorubicin and cisplatin, in separate mixtures with mAb 108 against KB cell tumors in vivo. See Hurwitz WS at ¶¶ 75-76; Pirak WS at ¶ 111. Significantly, these two mixture experiments did not function as controls to the conjugate studies, but were rather a wholly new experiment that Hurwitz proposed upon reviewing the results Pirak had observed

while Hurwitz was on sabbatical.[51] See Pirak WS at ¶ 112-13; Hurwitz ¶ 78.

In about March 1988, the Weizmann scientists discovered a synergistic effect when an unconjugated mixture of mAb 108 and either doxorubicin or cisplatin was administered to KB cells in vivo. See Pirak WS at ¶ 80; Hurwitz WS at ¶ 115; PTX006 Fig. 6. That is, when the mixture of mAb 108 and either of the cancer drugs was administered to the mice, "the effect on the tumor cells was more than merely additive and growth was significantly inhibited." Pirak WS at ¶ 80; see also PTX006 Fig. 6 (illustrating that the mixture's cytotoxic effect is greater than the effect of the antibody alone plus the effect of the drug alone). This discovery would later form the basis for the '866 patent.

H. The 1988 Paper

In early 1988, the Weizmann scientists began preparing a paper in order to publish the results of their experiments with mAb 108 and cisplatin.[52] See Pirak WS at ¶ 124. Initially, they

[51] This fact is clear for two reasons: first, mixtures involving cisplatin could not serve as controls to conjugate studies that did not include cisplatin at all; second, the Weizmann scientists had laid out a protocol with four controls, as reflected in the March 1987 report, see PTX047, none of which involved a mixture of a free drug and mAb 108.

[52] Although the Weizmann scientists also observed synergy in the mixtures of mAb 108 and doxorubicin, they decided that they would only publish the results obtained with cisplatin, which compared slightly

decided to publish two articles: the first would contain the in vivo results observed in the tests with mAb 108 by itself, while the second would include the data reflecting the synergy observed in the mixture experiments. See id. at ¶ 125. Pirak drafted the first paper, which was edited by Hurwitz and Sela, who also held several meetings with Pirak to discuss the paper. See id. at ¶ 126-27.

In March 1988, Schlessinger visited the Weizmann to deliver a lecture, which Pirak attended. See id. at ¶ 127. Pirak had previously scheduled a meeting with Sela that day to discuss a draft of the paper, and she approached Schlessinger after his lecture to invite him to attend "[b]ecause of [his] expertise and research interest in EGF and the EGF receptor, and because he had provided us with mAb 108 . . . ." Id. at ¶ 127. Schlessinger agreed to attend, and later that day, he, Pirak, and Sela met in Sela's office to discuss the research performed by the Weizmann scientists. See id. at ¶ 128. As noted earlier, at this point, Pirak's draft only discussed mAb 108. See id. at ¶ 129. However, the Weizmann scientists had already observed the synergy by this time, and Pirak brought the raw data reflecting the synergy to the meeting with Sela, Hurwitz,

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favorably with those obtained with doxorubicin. See Pirak WS at ¶ 119.

and Schlessinger.[53] See id. At some point during this meeting, Sela, Pirak, and Schlessinger agreed that the initial paper should reflect the results of the mixture experiments. See Pirak WS at ¶ 131. Also during this meeting, Schlessinger requested that Pirak and Sela send him a write-up of the results. See PTX069; PTX070. However, at no point did Schlessinger inform the Weizmann scientists that he intended to seek a patent based upon the research they had performed. See Pirak WS at ¶ 134. Subsequently, on April 26, 1988, Hurwitz sent Schlessinger a letter, in which she stated that she wished to inform him "of our latest results using [mAb 108] in combination with [doxorubicin] and cisplatin against KB cells." PTX069. Hurwitz attached to that letter a summary of the results observed by the Weizmann scientists in the form of a three-page document with several graphs depicting the synergy they observed in the mixture experiments. See PTX070.

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[53] Schlessinger testified that he recalled learning of the synergy from Hurwitz shortly before this meeting, see Schlessinger WS at ¶ 67, while Pirak believes that Schlessinger first learned of it at this meeting. See Pirak WS at ¶ 128. Schlessinger testified in his witness statement that, "I periodically communicated with Dr. Hurwitz and was kept apprised of the data she generated . . . ." Schlessinger WS at ¶ 66. Hurwitz, meanwhile, testified that "[t]hroughout the time we were actively doing this new research using mAb 108, I did not consult with Professor Schlessinger . . . ." Hurwitz WS at ¶ 84.

We do not credit Schlessinger's allegation that he communicated with Hurwitz, as it is wholly unsubstantiated by any contemporaneous records. Moreover, Schlessinger did not specify what data Hurwitz shared with him, such that even if the allegation were true, it would not affect our analysis.

Subsequent to drafting the paper and sending it to Schlessinger in April 1988, Pirak prepared several additional drafts, containing the results obtained both from mAb 108 alone and those obtained from the mixtures of 108 and cisplatin. See PTX161; PTX67. In July 1988, Pirak submitted a draft article to the Journal of the National Cancer Institute ("JNCI"), a peer-reviewed publication. See Pirak WS at ¶ 135. On August 15, 1988, the JNCI accepted the article for publication. See PTX075. After the Weizmann scientists responded to the JNCI reviewer's comments, see PTX160, Sela sent the finished paper to the JNCI Editor-in-Chief on September 2, 1988. See PTX077. The paper was published on December 21, 1988 with the title "Efficacy of Antibodies to Epidermal Growth Factor Against KB Carcinoma and in Nude Mice." See PTX006. The authors were listed as follows: Esther Aboud-Pirak, Esther Hurwitz, Michael Pirak,[54] Francoise Bellot, Joseph Schlessinger, and Michael Sela.[55]

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[54] Michael Pirak is Esther Aboud-Pirak's husband. He was listed as an author because he assisted in "handling the animals" used in the experiments, as well as in some other aspects of the experiments relating to the animals. See Pirak WS at ¶ 141(B). Because nobody alleges that he should be listed as inventor of the subject matter of the '866 patent due to this contribution, we need not discuss his role further.

[55] The Court heard a great deal of testimony relating to the significance in the scientific community of the order in which authors are listed on published papers, with most witnesses in agreement as to the conventions of the type of contributions to a research project that entitle one to authorship, and in what order the authors should

The Weizmann scientists submitted a second paper, entitled "Inhibition of human tumor growth in nude mice by a conjugate of doxorubicin with monoclonal antibodies to epidermal growth factor receptor," to the Proceedings of the National Academy of Science (the "PNAS") in 1989. See PTX007. This paper listed the same authors as the 1988 paper and discussed the results obtained with conjugates, rather than mixtures, of mAb 108 and doxorubicin. See id. A short time later, Pirak presented the results published in the 1988 and 1989 articles at a weekly meeting of the Weizmann Chemical Immunology Department. See Pirak WS at ¶ 140; PTX247.

III. PROCEDURAL HISTORY

A. Patent Application Process

1. Rorer Learns of the Discovery

Schlessinger testified at his deposition that "as soon as" he received the write-up of the results obtained by the Weizmann scientists, Rorer began working on a patent application. Schlessinger Dep. 127 lines 6-7. Although Schlessinger testified that he "was very pleased with the results" of the

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be listed. Specifically, it was generally agreed that the person who performed most of the hands-on research should be listed first, while the person who oversaw or supervised the research project should be listed last.

We find it unnecessary to discuss this issue further in our findings of fact, because the basis for listing scientists as authors of papers is altogether different from the legal basis for determining proper inventorship.

experiments at the Weizmann, "because they confirmed [his] belief that the co-administration of monoclonal antibodies to EGFR together with an anti-neoplastic agent was highly effective in treating certain cancers and reducing certain tumor cells," Schlessinger WS at ¶ 70, there is absolutely no documentary evidence substantiating the notion that Schlessinger held such a belief prior to receiving the results of the Weizmann scientists' experiments. Moreover, Schlessinger characterized the discovery of the synergy as a "surprise" on cross-examination, albeit a "minor" one, Tr. 529 lines 2-6, as did defendants in the patent itself. See PTX001-022 (stating that the named inventors "surprisingly discovered" the synergy).

Schlessinger shared the Weizmann results with Dr. Givol, who personally reported them to Rorer's CEO, Mr. Cawthorne, and Rorer's head of research, Dr. Tretter, at "about that time." See Tr. 725 line 2 to 726 line 11. A Rorer internal memorandum dated June 13, 1988, sent to Schlessinger, Kris, and one other Rorer employee, Mike Hrinda, reflects that a Rorer employee named Criss Tarr ("Tarr") performed a literature search "for studies of EGF receptor-tumor cell interactions" at the request of the memorandum's recipients. See PTX072-001. Specifically, Tarr suggested that the attached results of his search "could be used in IND preparation for clinical studies testing the utility

of anti-EGF receptor monoclonal antibodies in tumor therapy."[56] Id. Schlessinger acknowledged that this memorandum demonstrates that, "within a matter of weeks . . . after the results of the tests performed by Pirak and Hurwitz and Sela had landed on [his] desk at Rorer, the company was beginning to talk about going to the FDA and getting approval for this." Tr. 630 line 24 to 631 line 4. Simultaneously, Rorer "began to scale up to produce large quantities of the antibody [mAb 108]," anticipating that it would perform clinical trials. Tr. 631 lines 5-7.

On September 13, 1988, about two months after a draft of the 1988 paper was submitted for publication, Rorer held a management committee meeting, in which it discussed the status and goals of certain projects. See PTX293. Under the heading "Category A (High Priority) Projects" is listed "EGF Receptor Antibody," which refers to mAb 108. See id; Tr. 917 lines 3-5. Under the heading "Objective" for the mAb 108 project is the statement, "File IND by 7/89." See PTX293. Dr. Schreiber, who gave the status report at this meeting, testified that filing an IND in under ten months was "probably a little aggressive." Tr. 917 line 22. Moreover, he testified that it would be "logical"

[56] "IND" is short for "investigational drug application." Tr. 630 lines 18-19. Before seeking approval of a new drug from the FDA, applicants are first required to submit an IND. See Tr. 630 lines 14-23.

to seek a patent at the same time because a company would not want to "invest large resources" in the IND filing process "unless you had some idea of how you were going to ultimately protect the product if it were to become commercialized." Tr. 918 lines 21-23. Twelve days after this meeting, on September 25, 1988, Rorer's in-house lawyer, G.W. Rudman, sent a memorandum to Schlessinger, Givol, Kris, Bellot, and Schreiber[57] stating that Rorer had filed a patent application for a "Monoclonal Antibody Specific to Human Epidermal Growth Factor Receptor and Therapeutic Methods Employing Same." See PTX039.

Subsequently, in a later dated October 10, 1988, Rorer's Director of Biotechnology, George Gray ("Gray"), sent a letter to Dr. John Mendelsohn ("Mendelsohn") of the Memorial Sloan Kettering Cancer Center in New York, in "follow[] up" to conversations Mendelsohn had with Schlessinger and another Rorer employee, Tarr, about mAb 108. PTX079. The letter recites that Tarr "is sending you a 5 mg sample of the 108 antibody for evaluation," and that Gray "anxiously await[s]" the results of Mendelsohn's tests. PTX079. Specifically, the letter refers to Mendelsohn engaging in "clinical investigation of this antibody" in advance of "an IND filed by next spring." Id. Mendelsohn subsequently performed experiments with mAb 108, in which he

[57] The memorandum was also sent to George Gray, the Director of Biotechnology at Rorer. See PTX039; see also PTX079-002.

observed the same synergy observed by the Weizmann scientists when mAb 108 was administered in a mixture with anti-cancer drugs.[58] See Tr. 521 line 14 to 522 line 17.

Despite Rorer's contention that it lacked the facilities to perform animal tests, a memorandum dated October 28, 1988, reveals that it intended to perform in-house tests with mAb 108 on "mice, rats, rabbits, and primates," in advance of filing its IND. See PTX082-002; Tr. 922 lines 8-23. Schreiber testified that these were only "safety tests," which are "very different than establishing proof of concept or efficacy in animal models." Tr. 922 lines 17-21. He explained that Rorer's animal testing facilities were "dedicated for the safety testing of agents under development." Tr. 922 lines 18-19. Regardless, the record is clear that as soon as Rorer's management learned of the results of the tests performed by the Weizmann scientists with mAb 108, they immediately began pursuing patent protection with an eye toward developing the antibody for therapeutic use.

On July 1, 1988, within several weeks of Schlessinger's receipt of the results obtained by the Weizmann scientists, Eugene Moroz ("Moroz") and John Bauer ("Bauer"), two patent attorneys from the law firm of Morgan & Finnegan who served as

[58] As noted earlier, the antibody eventually marketed as Erbitux is actually C225, a monoclonal antibody created by Mendelsohn in 1983 (three years before mAb 108 was created), and which possesses the same relevant properties as mAb 108. See Tr. 524 lines 7-17.

outside counsel to Rorer, met with Rorer representatives in King of Prussia, Pennsylvania. See Tr. 1055 line 24 to 1056 line 14. During that meeting, "there was a discussion as to whether certain individuals," namely, the Weizmann scientists,[59] "should or should not be named as inventors." Tr. 1059 lines 10-13. Based on that discussion, the patent attorneys determined that the Weizmann scientists should not be listed as inventors. See Tr. 1060 line 14 to 1061 line 5. Significantly, none of the Weizmann scientists were ever consulted to determine their contributions to the claims made in the subsequent patent application. Moreover, Moroz testified that during this meeting, he was not told "that the individuals in Israel had been working under the direction of someone called Joseph Schlessinger." Tr. 1068-1071.

Shortly after Rorer began the patent application process, it filed for an IND on November 20, 1989. See PTX092A. Significantly, the IND application specifically relies on Figure 1(B) from the 1988 paper in stating that mAb 108 "inhibited the binding of EGF to KB . . . cells." PTX092A-025. In its IND application, Rorer used an "exact copy" of Figure 1(B) from the 1988 paper without informing the Weizmann scientists or Yeda.

[59] Moroz remembered that the people they discussed adding to the patent were scientists from Israel, though he did not specifically recall their names. See Tr. 1050 lines 9-18. However, it is clear that the discussion concerned the Weizmann scientists.

Tr. 808 line 2. Thus, Rorer informed the FDA that Figure 1(B), a graph reflecting data generated entirely by the Weizmann scientists, demonstrates that mAb 108 inhibits the binding of EGF to its receptors on the surface of KB cells, despite its current position that Figure 1(B) does not demonstrate this. See PTX092A-025; see also Tr. 807 line 11 to 808 line 4. In fact, Rorer did not rely on any other source other than Figure 1(B) in representing to the FDA that mAb 108 inhibits the binding of EGF to EGFR. See PTX092A-025 to PTX092A-026.

2. The '737 Application

On September 15, 1988, Morgan & Finnegan filed U.S. patent application number 07/244,737 (the "'737 application"),[60] entitled "Monoclonal Antibody Specific to Human Epidermal Growth Factor Receptor and Therapeutic Methods Employing Same," naming Schlessinger, Givol, Bellot, and Kris as inventors. See PTX002A. The '737 application contained claims to mAb 108, as well as to various methods for treating human tumor cells with 108, including administering 108 along with doxorubicin or cisplatin. See PTX002A-023 to PTX002A-0028. The text and figures accompanying the '737 application were largely taken directly from the 1988 paper; indeed, the figures were literally cut out of a copy of the paper and inserted into the patent application. See Tr. 370 line 7 to 373 line 17 (Bauer

[60] The application was signed by Bauer.

acknowledging that the text of the '737 application was "lifted directly" from the 1988 paper and that the accompanying figures were "identical" to those in the 1988 paper). In short, the '737 application almost exclusively reflects information contained in the 1988 paper, which was drafted by the Weizmann scientists, and in many cases the '737 application literally copies the language of the 1988 paper. We have attached copies of the 1988 paper and the '737 application for illustrative purposes. Compare PTX006 with PTX002A.

The Patent and Trademark Office ("PTO") issued its first restriction requirement on the '737 application on May 7, 1991. See PTX-002-109 to PTX002-112. The PTO first classified the nineteen claims contained in the original application into three groups, stating that each group constituted a distinct claimed invention: Group I included those claims "drawn to monoclonal antibodies and hybridomas"; Group II covered "methods for inhibiting the growth of human tumor cells using monoclonal antibodies and and [sic] to therapeutic compositions"; and Group III included the claims "drawn to methods for inhibiting the growth of human tumor cells using monoclonal antibodies and anti-neoplastic agents and to therapeutic compositions."[61] PTX002-110. The restriction requirement obligated Rorer to make

[61] As discussed infra, the patent that eventually issued only involved claims originally found in Group III.

an election as to which group of claims to pursue.[62] Subsequently, on May 31, 1991, Rorer elected to pursue the Group I claims drawn to monoclonal antibodies and hybridomas. See PTX002-113.

On July 12, 1991, the PTO rejected the claims in Group I, concluding, inter alia, that the claims were "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." PTX002-119 (citing 35 U.S.C. § 112). After Rorer failed to respond to this rejection, the PTO issued a notice of abandonment of the '737 application on February 12, 1992. See PTX002-128.

3. The '109 Application

On March 3, 1989, Bauer filed U.S. patent application number 07/319,109 (the "'109 Application") on Rorer's behalf as a continuation-in-part ("CIP") of the '737 application.[63] PTX003-005 to PTX003-059. The '109 application contained all

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[62] Restriction requirements are imposed when the patent examiner determines that a patent application contains more than one purported invention, as an issued patent may only cover one distinct invention. See In re Longi, 759 F.2d 887, 892 (Fed. Cir. 1985).

[63] A continuation-in-part, or CIP, is a "successor patent application" that is filed in order to either supplement an existing application with "some additional disclosure . . . over and above what was contained in the parent application," or to remove something. See Tr. 1063 line 19 to 1064 line 15. Any information revealed in a CIP dates back to the date of the parent application for purposes of determining priority of patent applications. See Tr. 1070 line 5 to 1071 line 5.

nineteen of the claims originally contained in the '737 application, as well as eleven new claims drawn to mAb 96. See PTX003-031 to PTX003-038. On July 31, 1990, the PTO issued another restriction requirement, concluding that the '109 application contained two inventions that are "distinct, each from the other." PTX003-061. Specifically, the PTO stated that the application contained two groups of claims: the first related to claims "drawn to monoclonal antibodies and hybridomas," while the second included claims "drawn to methods for inhibiting growth of human cancer cells using monoclonal antibodies with anti-neoplastic agents and to therapeutic compositions containing monoclonal antibodies and monoclonal antibodies plus anti-neoplastic agents." Id. In the same office action, the PTO issued a rejection of those claims drawn only to the monoclonal antibodies and hybridomas, consistent with its earlier rejection of similar claims contained in the '737 application. See PTX003-060; PTX003-071 to PTX003-074. The PTO predicated its rejection on, inter alia, the fact that these claims were either "anticipated by" earlier papers by Sato et al. and Rodeck et al., see 35 U.S.C. § 102(b), or were rendered obvious by those same papers, as defined by 35 U.S.C. § 103. See PTX003-072.

Rorer responded to this office action on November 30, 1990 by arguing that the claims drawn to monoclonal antibodies and

hybridomas were improperly rejected, as mAbs 96 and 108 were substantially different from previous monoclonal antibodies. See PTX003-094 to PTX003-106. On March 18, 1991, the PTO reiterated its rejection, stating that these claims "remain rejected under 35 U.S.C. § 102(b)/103 over Sato et al. or Rodeck et al." PTX003-137. The PTO explained that these two references "teach EGFR-specific monoclonal antibodies which bind to the extracellular domain of human EGFR and inhibit growth of human cancer cells stimulated by low concentrations of EGF," and that Rorer's attempts to suggest properties of their antibodies distinct from the ones disclosed by Sato and Rodeck were unconvincing, as those properties were "inherent in the referenced antibodies in the absence of evidence to the contrary." Id.

Rorer responded to this rejection on June 18, 1991 by requesting reconsideration, insisting that the PTO's rejection "is based on an inference of biological properties in the referenced antibodies which inference is unsupported by any evidence." PTX003-152. The PTO disagreed, and subsequently issued its fourth rejection to Rorer's attempts to patent its monoclonal antibodies and hybridomas on June 28, 1991. See PTX003-158 to PTX003-161.

4. The ’852 Application

On September 17, 1991, Rorer filed U.S. patent application number 07/760,852 (the “’852 application”) as a CIP of the ’109 application. See PTX003-167. This application, the third in the chain leading to the ’866 patent, contained a total of thirteen claims, again including claims drawn solely to the monoclonal antibodies and hybridomas. See PTX003-167 to PTX003-191. On December 29, 1992, the PTO again rejected those claims drawn to the monoclonal antibodies and hybridomas, the fifth occasion on which the PTO rejected such claims. See PTX003-198. Rorer failed to respond to this rejection and, on August 9, 1993, the PTO issued a notice of abandonment of the ’852 application. See PTX003-214.

5. The ’411 Application

Rorer filed U.S. patent application number 08/086,411 (the “’411 application”) on June 29, 1993, as a CIP of the abandoned ’852 application. See DTX131. The ’411 application added Ricca, Cheadle, and South to the application due to their work relating to the sequencing of the antibodies referenced in the application. See DTX131-1. This application contained six claims, four of which related to monoclonal antibodies and hybridomas, and the other two relating to a method for inhibiting tumor cell growth by administering an effective amount of a monoclonal antibody. See id. On November 4, 1993,

Rorer amended the '411 application to include claims to methods for inhibiting the growth of human tumor cells by administering a monoclonal antibody along with an anti-neoplastic agent. See DTX131-04.

On March 28, 1994, the PTO issued a restriction requirement, concluding that the '411 application included three groups of inventions: Group I included claims "drawn to monoclonal antibodies and hybridomas"; Group II included claims "drawn to methods for inhibiting the growth of cells that express human EGFR and therapeutic compositions"; and Group III included claims "drawn to cDNAs encoding the variable regions of monoclonal antibodies 108 and 96," referring to the contributions of Ricca, Cheadle, and South. PTX004A-003. The PTO also rejected two of the claims in Group II, stating that an earlier monoclonal antibody created by Rodeck et al., known as mAb 425, "appears to be the same or at least, functionally equivalent to the monoclonal antibody 108 which is used in certain embodiments of the claimed invention." PTX004A-016. Finally, and perhaps most significantly in the context of the instant dispute, the PTO rejected all but two of the claims in the '411 application under 35 U.S.C. § 102(f) for improper inventorship. See PTX004A-012. Specifically, the PTO stated:

> Claims 12, 14 and 15 rejected [sic] under 35 U.S.C. § 102(f) because the applicant did not invent the claimed subject matter as

> evidenced by Aboud-Pirak et al. (J. Nat'l. [sic] Cancer Inst. 80).
>
> Aboud-Pirak et al. teach a composition comprising monoclonal antibody 108 and the anti-neoplastic agent cisplatin (see page 1607).
>
> The reference raises a question with respect to the inventorship of the claimed invention because it names six co-authors, only two of whom are named inventors herein . . . . Because of this ambiguity, it is incumbent on applicants to provide a satisfactory showing which would lead to a reasonable conclusion that applicant alone is the inventor of the claimed invention. In re Katz [sic], 687 F.2d 450, 215 USPQ 14 (CCPA 1982). To resolve the ambiguity, applicants may file declarations by the non-applicant co-authors of the reference disclaiming the invention or a declaration by applicant setting forth the facts which provide an explanation as to why the non-applicant co-authors are not inventors.

PTX004A-12 to PTX004A-13. The PTO similarly rejected other claims in the '411 application, raising concerns about improper inventorship in light of the 1988 and 1989 papers by Pirak et al. See PTX004A-12 to PTX004A-16. Thus, the PTO informed Rorer that it would have to satisfactorily demonstrate sole inventorship of the method claims in order to obtain a patent. Despite the suggestion that Rorer obtain affidavits from the Weizmann scientists disavowing their patent rights, Rorer, and later, ImClone, declined to do so.

Shortly after this PTO action, ImClone approached Rhône-Poulenc Rorer, Inc. ("RPR") about entering into an agreement

whereby ImClone would take over prosecution of RPR's pending patent application and would enter into an exclusive licensing agreement, enabling ImClone to develop a commercial product based on the C225 antibody created by Mendelsohn. See Gallagher WS at ¶¶ 4-5. In June 1994, ImClone and RPR signed such an agreement, which included both upfront cash payments and royalty payments upon the introduction of a commercial product. ImClone immediately took over the patent prosecution. See id. at ¶ 5; DTX39. The agreement also specified that RPR was permitted to pursue any claims abandoned by ImClone, but, as noted below, RPR declined to pursue any of the claims abandoned by ImClone, including those claims drawn solely to mAb 108.

Subsequently, ImClone responded to the March 28, 1994 office action, stating, inter alia, that mAb 108 was sufficiently different from previous monoclonal antibodies to be independently patentable. See PTX004B-011. Moreover, ImClone stated that the applicants would submit a declaration explaining why the Weizmann scientists should not be considered inventors. Specifically, ImClone stated, "Applicants solely conceived of the research project that resulted in the data published in the cited journal articles [referring to the 1988 and 1989 papers], the results of which are included in the subject matter of the subject application. Applicants will submit the Declaration stating these facts as soon as possible." PTX004B-010. While

ImClone subsequently drafted such a declaration, it was never submitted to the PTO. Tr. 1166 lines 5-19. Moreover, Thomas Gallagher, the Vice President of Intellectual Property at ImClone and the company's Rule 30(b)(6) designee, testified at his deposition that "speaking for ImClone[,] [t]he company does not know" the basis for the statement that the applicants "solely conceived of the research project," though that statement later formed the basis for its patent application. Gallagher Dep. Tr. 97 lines 6-19. Moreover, Gallagher was not aware of any effort made by ImClone to confirm that the named inventors were the actual inventors before prosecuting the patent. See Tr. 1168 lines 3-13.

On January 19, 1995, the PTO issued an office action in which it maintained its rejections under 35 U.S.C. § 102(f), as the applicants had failed to submit the requested declaration. See DTX131-12. Moreover, the PTO again rejected the claims drawn to mAb 108 as insufficiently distinct from monoclonal antibodies previously created by other scientists. See id. ImClone failed to respond to this office action, and on August 29, 1995, the PTO filed a notice of abandonment for the '411 application. See DTX131-13.

6. The '761 Application and the Issuance of the '866 Patent

On June 7, 1995, ImClone filed U.S. patent application number 08/487,761 (the "'761 application") as a CIP of the '411

application, listing the named inventors alongside Ricca, Cheadle, and South, despite the fact that the application did not contain claims drawn to the cDNA, which related to Ricca, Cheadle, and South's work.[64] See PTX005. The '761 application contained the same six claims as the originally filed '411 application: four drawn to the monoclonal antibodies and hybridomas and two drawn to a method for inhibiting tumor cell growth by administering monoclonal antibodies. See PTX005-046 to PTX005-047. On September 5, 1997, the PTO rejected all six claims under 35 U.S.C. § 102(a) as being anticipated either by an article by Ennis et al. or by the 1988 paper. See PTX005-133. The PTO also rejected the independent claims drawn to both the monoclonal antibodies and the method for their use under 35 U.S.C. § 102(b) as anticipated by either Mendelsohn et al. or Murthy et al., who had both published papers disclosing antibodies with the same fundamental characteristics as mAb 108. See PTX005-134. Moreover, the PTO rejected the remaining claims drawn to the specific hybridoma cell line that produced mAb 108, stating that "the record does not contain any evidence that the cell line differs in any significant manner or produces a monoclonal antibody that differs in any significant aspect from

[64] During the pendency of the '761 application, ImClone also filed U.S. patent application number 09/652,649 (the "'649 application") as a CIP of the '761 application. See PTX139. However, in October 2000, ImClone withdrew the '649 application before the PTO had examined it. See PTX137; PTX138; Tr. 1210 lines 5 to 18.

hybrid cell lines that are taught in either of Mendelsohn et al. or Murthy et al." PTX005-135.

In response to this rejection, on March 5, 1998, ImClone withdrew the six original claims contained in the '761 application and substituted seventeen new claims. In addition to claims drawn to the hybridomas and monoclonal antibodies, ImClone resubmitted claims drawn to the cDNA work done by Ricca, Cheadle, and South, as well as claims directed to a method for treating cancer by administering a monoclonal antibody and an antineoplastic agent. See PTX005-145. ImClone also responded to the previous rejections made to the '411 application under 35 U.S.C. § 102(f) before it was abandoned, arguing that In re Katz was inapplicable, as it involved "journal articles that were published before the filing date of a patent application." PTX005-152. Here, ImClone pointed out that "the Aboud-Pirak articles can be avoided simply by referring to the earlier filing date of the original priority application," such that the § 102(f) rejection was improper. See id. ImClone failed to disclose, however, that the named inventors were in possession of the 1988 paper well before it was published. Regardless, ImClone argued that it should not have to submit the type of declaration suggested in In re Katz,[65] as the 1988 and 1989

[65] Although defendants made several arguments during trial regarding the significance of the section under which the PTO rejected its

papers were published after the original filing date of the chain of applications leading to the instant application. See PTX005-153.

On September 11, 1998, the PTO again rejected claims drawn to the monoclonal antibodies and hybridomas and issued a further restriction requirement, determining that fourteen of the seventeen claims were required to be withdrawn "as being directed to a non-elected invention." PTX005-166. This rejection again cited prior literature by Mendelsohn et al. and Murthy et al. in determining that claims drawn to mAb 108 were anticipated by other scientists. See PTX005-167. Moreover, the rejection cited the 1989 paper as grounds for rejecting claims drawn to mAb 96. See PTX005-167.

On February 12, 1999, ImClone requested reconsideration of the September 11, 1998 office action. See PTX005-176. On May 13, 1999, the PTO responded, issuing a restriction requirement that required ImClone to elect to prosecute one of three groups of claims: Group I included method claims involving the administration of a monoclonal antibody and an anti-neoplastic agent to tumors; Group II included claims drawn to hybridoma cell lines; and Group III included claims drawn to cDNA

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claims, our analysis is not affected by this issue. We recite these facts in order to illustrate that defendants represented to the PTO that a declaration was unnecessary due to the date on which the 1988 paper was published, while failing to inform the PTO that the application was derived from a draft of the paper received well before its publication date.

sequences. See PTX005-292. ImClone responded eleven days later by electing to prosecute the Group I claims, for which it requested another review in light of the arguments it raised relating to those claims in its submission of February 12, 1999. See PTX005-294. On September 28, 1999, the PTO rejected the two remaining independent claims under 35 U.S.C. § 102(b) as anticipated by a paper by Epenetos. See PTX005-298 to PTX005-299. The other claims, all of which were dependent on the claims rejected under § 102(b), were likewise rejected. See id.

ImClone's response to this rejection was to add a claim limitation requiring that the monoclonal antibodies "inhibit binding of EGF to the receptor." PTX005-315. This limitation was added pursuant to patent "[e]xaminer Johnson's suggestion" during an in-person interview held between representatives of ImClone and examiner Johnson, in which ImClone sought suggestions on how to distinguish its patent application from a patent obtained by Hudziak et al. (the "Hudziak patent").[66] PTX005-316; Tr. 1212 lines 11-21. This was the first occasion on which this claim limitation appeared in one of the chain of applications eventually leading to the issuance of the '866

[66] On cross-examination, Gallagher acknowledged that the Hudziak patent was an "unwelcome discovery for ImClone." Tr. 1189 lines 13-15. Gallagher's efforts to "get behind the filing date" of the Hudziak patent, i.e., prove that the subject matter of the '866 patent antedated Hudziak's work, led to his decision to send Sela the email that put plaintiff on notice of defendants' patent application, as discussed infra. See Tr. 1192 line 5 to 1193 line 3.

patent, appearing as the claim limitation embodied in element (iii) of Claim 1, as well as in Claim 6 of the issued patent.

As Gallagher explained at trial, in order to add a limitation to a pending application and have it date back to the date of the original filing, an applicant must demonstrate that support for the limitation was fully disclosed in the original application. See Tr. 1215 line 15 to 1216 line 8. As support for the limitation, ImClone offered as its first citation "page 14, line 13 et seq." of the original specification. See PTX005-308. This citation refers to the text accompanying Figure 1(B) of the 1988 paper, which was copied into the original application and labeled Figure 2. See Tr. 1217 line 19 to 1219 line 14. Thus, the applicants specifically cited Figure 1(B) of the 1988 paper as support for the proposition that mAb 108 inhibits the binding of EGF to EGFR. After this limitation was added, the PTO issued a notice of allowability, holding that the remaining nine claims, all of which were drawn to a method of administering a monoclonal antibody and an anti-neoplastic agent, were patentable. See PTX005-328. After renumbering the claims 1-6 and submitting new drawings, the '866 patent application issued on April 17, 2001. See PTX001.

C. Yeda Learns of the Patent Application

1. Yeda's Patent Policies

It was not Yeda's practice in the period relevant to this case to track published patent applications and issued patents in the ordinary course of business. See Mirelman WS at ¶¶ 19-20. Prof. Mirelman, who served on Yeda's board of directors from 1983 to 2005, testified that "Yeda's job was to manage inventions by obtaining patents and licensing them to commercial companies. It did not have the manpower or financial resources available to do such a search on a regular basis . . . ." See id. at ¶ 20. Moreover, we know of no reason why Yeda would have believed that RPR and ImClone were seeking to obtain a patent based on research performed by the Weizmann scientists, such that it should have been alerted to look for such a patent.

Mirelman also testified that "it was mostly the initiative of the scientists themselves to come to Yeda and disclose any developments they have made that in their view may merit patent protection." Mirelman WS at ¶ 10. Although the Weizmann had policies requiring its scientists to disclose any inventions, Mirelman explained that the Weizmann permits "each scientist [to] judge[] for himself whether or not there is an invention and whether or not a patent should be filed." Id. at ¶¶ 23-24. He further explained that although scientists "may be criticized for not . . . publishing enough," id. at ¶ 28, "all professors

have complete freedom to decide whether any new discovery would be referred to Yeda for a possible patent application and there are no repercussions or punishment for not disclosing an invention." Id. Significantly, scientists at the Weizmann are given no training in patent law. See id. at ¶ 29.

Sela testified that although he "had 372 original articles and probably another 200 books and books that [he] edited, reviewed, and so on," he was named only on "something like 20 [patents], of which more than half is all around Copaxone." Tr. 343 lines 6-10. As Sela explained on cross-examination, he sometimes "forget[s] to think that [an invention] is something that could be patented," Tr. 349 lines 12-13, and, in this specific instance, stated: "I don't mind if I don't take a patent, unless it's stolen from me."[67] Tr. 344 lines 13-14. Here, Sela decided not to pursue a patent, since he "believed that because mAb 108 was provided by Prof. Schlessinger while he was on his sabbatical at Meloy, if a patent was to be taken out, it would have to involve approval and prosecution in cooperation with Meloy," such that he "had no great wish to go through what [he] perceived would be a fairly complicated and involved process of negotiating and discussing a potential patent

[67] We fully credit Sela's testimony that: "As a scientist and professor of an academic institution, my primary goal is and has always been to do interesting, exciting and cutting edge research and publish, for the scientific community to learn, and to invite discourse and advance science in the field I choose to work [sic]." Sela WS at ¶ 58.

application and license of the invention." Sela WS at ¶ 60. Moreover, Sela "assumed that if Prof. Schlessinger or others at Meloy wanted to apply for a patent, he would contact [Sela] to discuss the issue. Since Prof. Schlessinger did not do so, [Sela] was perfectly happy to let the discoveries be disseminated to the public." Id. In short, we credit Sela's testimony that he decided not to pursue a patent not because he did not believe he was entitled to one, but rather because he was comfortable disseminating the information he had discovered to the public through the published papers.

2. First Notice of the Patent Application

On January 10, 2000, Gallagher, ImClone's patent counsel, sent Sela an email in which he referred to "work developed by Josef Schlessinger . . . demonstrat[ing] the therapeutic effect of combining anti-EGFR antibodies with chemotherapeutic drugs." DTX282-IMC03307. Gallagher explained that due to "developments in the prosecution of a US patent application claiming this combination," he desired to "examine notebook records that describe various aspects of the Invention," which he believed to be in the possession of Sela and his colleagues. Id. Because Sela was "completely unaware of any patent application on the work described in the 1988 article," he requested that Yeda "follow up on the communication from Mr. Gallagher" and "perform

a search" for the patent application.[68] Sela WS at ¶¶ 69-70. Yeda did not find the application, prompting Nechama Bassewitch Frankel ("Frankel"), a lawyer for Yeda, to email Gallagher on January 25, 2000, stating that Yeda was "not aware of any invention claimed on the research performed at the Weizmann on the subject." DTX282-IMC03308. Frankel specifically requested that Gallagher provide her with "any information on the subject" that he possessed.[69] Id.

As of March 20, 2000, Gallagher had yet to respond to Frankel's email, leading Frankel to follow up with another email, in which she stated that she was "quite disturbed by the fact that [she had] received no respond [sic] to [her] email message of January 25th." DTX282-03309. Gallagher sent a short response to Frankel on April 6, 2000, apologizing for the delay in responding, and explaining that his "inquiry became irrelevant in light of other developments," which he declined to

[68] Sela also testified that he contacted Schlessinger, who gave him "an ambiguous and contradictory answer," namely that "no patent existed, but that if there was a patent he was not receiving any money from it." Sela WS at ¶ 69. Though we credit Sela's recollection that such a conversation occurred, it plays no role in our analysis.

[69] We note that some point after Sela received the initial email from Gallagher, he contacted Hurwitz to see if she could locate her notebooks from the relevant time period. Hurwitz then learned that her notebooks, along with Pirak's, had been misplaced or thrown away. See Hurwitz WS at ¶ 9. Defendants suggested at trial that the misplacing of these notebooks somehow prejudiced them. See Def. Mem. of Law at 43. However, we are unsure what information these notebooks might have contained that was not amply substantiated at trial by other evidence, especially the published articles, and defendants do not suggest how the absence of these notebooks prejudiced them.

specify. DTX282-03310. Frankel replied four days later, changing the subject line of the email to "irrelevant to who? [sic]" and stating that her "queries still remain." DTX282-03311. Frankel continued, "Please, though you are not concerned, I would like to clear mine [sic]." Id.

The last email in the exchange was sent by Gallagher to Frankel on April 18, 2000. See DTX282-03312. In that email, Gallagher stated:

> At the time of my initial inquiry to Dr. Sela I was trying to determine the date that a specific Rhone-Poulenc antibody was first used in experiments, which Dr. Schlessinger may have had done at the Weizman [sic] Institute while he was an employee of Rhone-Poulenc. Just at the time of your initial contact with me I was able to resolve this issue without having to recontact the Weizman [sic] Institute.

Id. Gallagher testified that, "[i]n the year 2000, U.S. [patent] applications were not publicly available," such that he thought he was "providing Ms. Frankel with all of the information that [he] reasonably could have other than a serial number."[70] Tr. 1203 lines 14-17. However, Gallagher testified that there was "nothing in the law" that prevented him from sharing more information with Frankel, and that he was "perfectly free to tell someone else about a pending U.S.

[70] Gallagher essentially contended that, despite the fact that defendants argue in this case that Yeda should have known about the patent application, he could not disclose its existence.

application" if he so desired. Tr. 1205 lines 1-4; Tr. 1206 lines 15-17.

On March 18, 2001, Mirelman spoke with Schlessinger about the patent application during a break in a conference being held at the Weizmann. See Mirelman WS at ¶ 33; see also PTX269 (conference poster). During this conversation, Schlessinger inquired about Dr. Sela and told Mirelman that he was not involved in ImClone's patent prosecution, specifically suggesting to Mirelman that Sela should be named on the patent. See id. at ¶ 35. Subsequently, on May 8, 2002, Prof. Haim Garty, then the Chairman of Yeda and the Vice President of the Weizmann Institute for Technology Transfer, held a meeting with Dr. Isaac Shariv ("Shariv"), then Yeda's CEO, and Professor Givol in order to discuss the '866 patent, which Yeda had recently located. See Garty WS at ¶¶ 3, 5-6. During this conversation, which Shariv contemporaneously memorialized with a typewritten document, Givol stated that he "did not have any true involvement in the project." PTX142 at ¶ 5. Moreover, Givol stated that he was unaware of any work at Rorer on the combination that formed the basis for the issued '866 patent. See id. at ¶ 8. Shortly thereafter, on June 3, 2002, Yeda held a meeting of its board of directors, at which the directors discussed Yeda's ownership rights in the patent. See Garty WS at ¶ 10; see also PTX143 (minutes of board meeting). During

that meeting, the directors decided that four board members, including Garty and Mirelman, would "initiate steps to claim Yeda's rights to the '866 patent." Id. at ¶ 15. This committee decided to organize a meeting with Aventis representatives, which was held on July 29, 2002 in New Jersey. See id. at ¶ 16. During this meeting, attended by Garty, Shariv, and Pirak as well as two Aventis representatives, Aventis agreed to review the inventorship question and to discuss Yeda's concerns with ImClone. See id. In order to assist Aventis, Yeda provided it with documents substantiating its inventorship claims under a non-disclosure agreement. See id. at ¶ 17.

The next day, Garty called Schlessinger to discuss the dispute. See Garty WS at ¶ 19. Within 24 hours of this conversation, Garty sent an email to Mirelman and Shariv summarizing the discussion. See id. at ¶ 23. In that summary, Garty quoted Schlessinger as telling him "of course Michael Sela should be on the patent." PTX144. Moreover, Schlessinger told Garty that he would be "prepared to testify in court that WIS scientists should be inventors on the patent." Id. Schlessinger also mentioned to Garty that, while he was entitled to no future royalties from Aventis, he should receive a part of any proceeds received by Yeda because he was a professor at the Weizmann. See id. Schlessinger testified that, although he remembered speaking to Garty on that date, he had no

recollection of any discussion about Sela or the inventorship dispute generally.[71] See Tr. 642 line 22 to 643 line 9. Mirelman, who had previously spoken with Givol about the dispute, replied to this email by telling Garty that he "was quite confident that Yossi [Schlessinger] would react as he did . . . ." PTX270.

D. Development and Commercial Success of Erbitux

On April 9, 1993, ImClone entered into a licensing agreement with the University of California, San Diego ("UCSD") to develop the 225 antibody created by Dr. Mendelsohn at UCSD.[72] See DTX773. ImClone then entered into an agreement with the National Cancer Institute, which had chimerized[73] the antibody.[74]

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[71] Schlessinger did not memorialize the contents of the conversation in a written document.

[72] Although the precise facts of the development of mAb 225 are not relevant here, the Court notes that the question of whether ImClone in fact obtained the right to develop and eventually commercialize 225 is the subject of a separate dispute in the District of Massachusetts. See Massachusetts Institute of Technology v. ImClone Systems, Inc., 04-CV-10884-RGS, 2006 WL 2121479 (D.Mass. July 28, 2006). In that case, plaintiff MIT and its licensee allege that ImClone's manufacture and distribution of 225 as Erbitux violates a patent owned by MIT. See id. at *1. On July 28, 2006, the Massachusetts Court denied ImClone's motion for summary judgment on the issue of patent exhaustion, concluding that its arguments contained a "gaping hole" and were "beyond the court's grasp." Id. at *2.

[73] Mendelsohn originally created a mouse antibody called M225. See Martell WS at ¶ 8. The National Cancer Institute then chimerized it, or made it part-human and part-mouse, such that it could safely be used in humans. See id. After chimerization, the antibody was referred to as C225. See id. at ¶ 9. For the sake of clarity, we simply refer to the antibody as mAb 225, with the understanding that ImClone developed the chimerized, rather than the murine, antibody.

ImClone proceeded to engage in clinical trials with mAb 225 to determine its effectiveness in treating certain type of human cancers. See Martell WS at ¶ 9. As discussed supra, ImClone entered into a licensing agreement with RPR in June 1994 in anticipation of offering the antibody alongside anti-neoplastic agents for cancer therapy. After roughly eleven years of clinical trials, the FDA approved Erbitux for treatment of colorectal cancer in February 2004, and on March 1, 2006, approved Erbitux for treatment of head and neck cancers. See id. at ¶ 12.

On September 19, 2001, ImClone entered into an agreement with the Bristol Myers Squibb Company ("BMS") to jointly commercialize Erbitux. See DTX109. Under the terms of the agreement, BMS agreed to pay ImClone up to $2 billion. See id.; see also Tr. 1104 line 5 to 1105 line 9. As of the time of the trial, ImClone had received "about 900 million" dollars from BMS, with the potential for more money in future incentive payments.[75] See Tr. 1105 lines 7-9. This figure represents more than four and a half times the $190 million ImClone had invested in research and development expenditures before the signing of

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[74] The Court was not provided with a copy of this agreement, though we do not doubt its existence.

[75] U.S. sales of Erbitux were $260.8 million in 2004 and $413.1 million in 2005. See Martell WS at ¶ 15; DTX938. ImClone continues to pursue FDA approval for additional indications, or uses, for Erbitux. See Martell WS at ¶ 15.

the agreement. See Martell WS at ¶ 6; Tr. 1105 lines 14-24. Significantly, of the $190 million, more than $145 million, or 76 percent, was invested after January 1, 2000, which is nine days before the email exchange began that first informed Yeda that ImClone had been pursuing a patent based on research performed by the Weizmann scientists. See Martell WS at ¶ 6.

DISCUSSION

In its amended complaint, Yeda seeks two remedies pursuant to 35 U.S.C. § 256: (1) to have the Weizmann scientists added to the '866 patent; and (2) to have the named inventors removed from the patent. Defendants argue that the '866 patent correctly reflects the actual inventorship and, alternatively, that the affirmative defense of laches bars plaintiff's claims. For the reasons discussed below, we find that the Weizmann scientists are the sole inventors of the subject matter of the '866 patent and that the laches defense does not bar Yeda from seeking to correct its inventorship.

I. Legal Standard

A. Inventorship Defined

"Conception is the touchstone of inventorship, the completion of the mental part of invention." Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1227-28 (Fed. Cir. 1994). The Federal Circuit has defined conception as "'the formation in the mind of the inventor, of a definite and permanent idea of

the complete and operative invention, as it is hereafter to be applied in practice.'" Id. at 228 (quoting Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1376 (Fed. Cir. 1986)). Conception of an invention can be said to have occurred "only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation." Burroughs Wellcome, 40 F.3d at 1228 (emphasis added)(citations omitted).

As the Federal Circuit elaborated in Burroughs Wellcome, "the test for conception is whether the inventor had an idea that was definite and permanent enough that one skilled in the art could understand the conception; the inventor must prove his conception by corroborating evidence, preferably by showing a contemporaneous disclosure." Id. at 1228. Until a party can "describe his invention with particularity . . . he cannot prove possession of the complete mental picture of the invention." Id. However, "an inventor need not know that his invention will work for conception to be complete," but rather "need only show that he had the idea; the discovery that an invention works is part of its reduction to practice." Id. (citations omitted).

B. Correction of Inventorship

"Patent issuance creates a presumption that the named inventors are the true and only inventors." Caterpillar Inc. v.

Sturman Industries, Inc., 387 F.3d 1358, 1377 (Fed. Cir. 2004) (citing Hess v. Advanced Cardiovascular Sys., Inc., 106 F.3d 976, 980 (Fed. Cir. 1997). However, a party may rebut this presumption by proving with clear and convincing evidence that he is entitled to be named as an inventor and thus should have been included on the patent.[76] See, e.g., Checkpoint Systems, Inc. v. All-Tag Sec. S.A., 412 F.3d 1331, 1338 (Fed. Cir. 2005). Moreover, although the failure to include an actual inventor on a patent is ordinarily grounds for invalidating that patent, 35 U.S.C. § 256 ("section 256") permits a court to order its correction instead.[77] See Checkpoint Sys., Inc., 412 F.3d at

[76] We note that plaintiff suggests its burden of proof is lesser than the clear and convincing standard regarding certain points of contention. Because we find by clear and convincing evidence that the Weizmann scientists are entitled to sole inventorship, we need not address these arguments.

[77] Section 256 provides:

> Whenever through error a person is named in an issued patent as the inventor, or through error an inventor is not named in an issued patent and such error arose without any deceptive intention on his part, the Director may, on application of all the parties and assignees, with proof of the facts and such other requirements as may be imposed, issue a certificate correcting such error.
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> The error of omitting inventors or naming persons who are not inventors shall not invalidate the patent in which such error occurred if it can be corrected as provided in this section. The court before which such matter is called in question may order correction of the patent on notice and hearing of all parties concerned and the Director shall issue a certificate accordingly.

1338 ("'If a patentee can demonstrate that inventorship can be corrected as provided by [35 U.S.C. § 256], a district court must order correction of the patent, thus saving it from being rendered invalid.'"(quoting Pannu v. Iolab Corp., 155 F.3d 1344, 1350 (Fed. Cir. 1998))).

C. Joint Inventorship

Because Yeda asserts two distinct causes of action, one seeking to add the Weizmann scientists to the patent and the other seeking to remove the named inventors, the Court may find that all of the purported inventors deserve to be listed on the patent, i.e., that the '866 patent is the product of joint inventorship. 35 U.S.C. § 116 ("section 116") provides in relevant part:

> When an invention is made by two or more persons jointly, they shall apply for patent [sic] jointly and each make the required oath, except as otherwise provided in this title. Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent.
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> . . . .
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> Whenever through error a person is named in an application for patent as the inventor, or through error an inventor is not named in an application, and such error arose without

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35 U.S.C. § 256.

> any deceptive intention on his part, the Director may permit the application to be amended accordingly, under such terms as he prescribes.

In order to establish joint inventorship, "there must be some element of joint behavior, such as collaboration or working under common direction . . . ." Kimberly-Clark Corp. v. Proctor & Gamble Distributing Co., Inc., 973 F.2d 911, 917 (Fed. Cir. 1992). "All that is required of a joint inventor is that he or she (1) contribute in some significant manner to the conception or reduction to practice of the invention, (2) make a contribution to the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention, and (3) do more than merely explain to the real inventors well-known concepts and/or the current state of the art." Pannu, 155 F.3d at 1351. However, "each of the joint inventors need not 'make the same type or amount of contribution' to the invention." Ethicon, Inc. v. United States Surgical Corp., 135 F.3d 1456, 1460 (Fed. Cir. 1998) (quoting section 116). Instead, each purported inventor "needs to perform only a part of the task which produces the invention." Id. To establish joint inventorship by clear and convincing evidence, a party may not rely solely on his own testimony or that of his purported co-inventors, but rather must offer corroborating evidence of conception. See id.

II. Analysis

In order to determine who should properly be named as the inventors of the '866 patent, the Court must begin "with a construction of each asserted claim to determine the subject matter encompassed thereby." Trovan Ltd. v. Sokymat SA, Irori, 299 F.3d 1292, 1302 (Fed. Cir. 2002) (citations omitted). After defining the invention, the Court "is then to compare the alleged contributions of each asserted co-inventor with the subject matter of the properly construed claim to then determine whether the correct inventors were named." Id. (citing Ethicon, 135 F.3d at 1462).

A. What is the Invention?

As discussed extensively in the background section, the '866 patent is drawn toward a method of inhibiting the growth of human cancer cells by administering a member of a particular class of monoclonal antibodies with an anti-cancer drug in an unconjugated mixture. As the Supreme Court observed in 1909 regarding method, or combination, patents:

> A combination is a union of elements, which may be partly old and partly new, or wholly old or wholly new. But, whether new or old, the combination is a means - an invention - distinct from them. They, if new, may be inventions and the proper subjects of patents, or they may be covered by claims in the same patent with the combination.

Leeds and Catlin Co. v. Victor Talking Machine Co., 213 U.S. 301, 318 (1909).

Only two of the nine claims of the '866 patent are independent claims, i.e., Claims 1 and 6 describe the invention, whereas the remaining dependent claims add limitations to those independent claims. See Curtiss-Wright Flow Control Corp. v. Velan, Inc., 438 F.3d 1374, 1380 (Fed. Cir. 2006)(discussing "the presumption that an independent claim should not be construed as requiring a limitation added by a dependent claim.")(citations omitted). Thus, Claims 4 and 9, which both specify the use of mAb 108 as a member of the specified class of antibodies, are to be construed in light of their dependence on Claims 1 and 6, respectively. As a consequence, when determining the contribution of each purported inventor to the '866 patent, we must view those contributions with an eye toward the independent claims, i.e, the claims drawn to a method of using a member of a class of monoclonal antibodies and anti-cancer drugs, rather than toward any member of that class or the drugs themselves.

Although the patent claims do not specifically reference the synergy observed by the Weizmann scientists, it is well-settled that "[a]rguments and amendments made during prosecution of a patent application must be examined to determine the meaning of terms in the claims." Rheox, Inc. v. Entact, Inc.,

276 F.3d 1319, 1325 (Fed. Cir. 2002). Consequently, when construing the claims of the '866 patent, we are mindful of the fact that the PTO allowed them in response to defendants' representations that they had discovered a "general phenomenon" of synergy when a member of the specified class of monoclonal antibodies was administered in an unconjugated mixture with one of the specified anti-cancer drugs. PTX005-153.

B. Who are the Inventors?

1. The Weizmann Scientists are Inventors of the '866 Patent

The Weizmann scientists have demonstrated by clear and convincing evidence that they conceived of all of the claims embodied in the '866 patent.[78] Specifically, the Weizmann scientists conceived of treating human tumor cells that are mitogenically stimulated by EGF by administering a monoclonal antibody that binds to human EGFR in an unconjugated mixture with an anti-neoplastic agent. As detailed in the facts section, the Weizmann scientists extensively characterized mAb 108's properties before creating a testing protocol in which they decided to use cancer cells that are mitogenically stimulated by EGF, namely KB cells. They also chose to focus on two antineoplastic agents, doxorubicin and cisplatin, as eventually reflected in dependent claims 2 and 3 of the '866

[78] We reserve our discussion of whether the Weizmann scientists conceived of element (iii) of Claim 1 for the section on judicial estoppel, infra.

patent. Moreover, after observing promising results with conjugates of mAb 108 and the drugs, they decided to test an unconjugated mixture of the antibody and drug, which were not part of the original experimental design. In short, the Weizmann scientists collectively conceived of each element of the two independent claims of the '866 patent.

In finding that the Weizmann scientists have proven their inventive contributions by clear and convincing evidence, we rely not only on their testimony, but also on the overwhelming amount of corroborating documentary evidence. The Federal Circuit applies a "rule of reason" analysis in order to determine whether a putative inventor has sufficiently corroborated his claim of prior conception. See Price v. Symsek, 988 F.2d 1187, 1195 (Fed. Cir. 1993). In undertaking this analysis, the Court must engage in "[a]n evaluation of all pertinent evidence . . . so that a sound determination of the credibility of the inventor's story may be reached." Id. (emphasis in original). Here, the Weizmann scientists have presented documentary evidence substantiating each step of the inventive process, in stark contrast to the dearth of evidence supporting the named inventors' version of events. First, the Weizmann scientists documented the process by which they arrived at the decision to test antibodies targeting human EGFR along with cancer drugs in their written proposals and reports to the

Yeda-Fund, including their decision to test KB cells. See PTX029; PTX041. Their first progress report also reflects their decision to switch their focus from using EGF as a carrier for antineoplastic agents to using monoclonal antibodies for that purpose. See PTX041. Second, Pirak extensively characterized both mAb 108 and KB cancer cells before conducting experiments with cisplatin and doxorubicin, as reflected in the 1988 paper. See PTX006. These preliminary experiments revealed that mAb 108 binds to the extracellular domain of human EGFR and that EGF inhibits the binding of mAb 108 to EGFR. Third, after performing some preliminary in vitro tests, the Weizmann scientists performed all of the in vivo experiments that support the claims of the '866 patent, developing a protocol for using mAb 108 as a carrier for anti-cancer drugs to treat human tumor cells implanted in nude mice. See PTX047; PTX006. The results of these experiments are also embodied in the 1988 paper. See PTX006. Finally, the 1988 paper corroborates the undisputed testimony that Hurwitz suggested the mixture experiment that forms the basis for the '866 patent after reviewing the data generated in Sela's laboratory while Hurwitz was on sabbatical. See id. Moreover, it is clear from the chronology that the mixture experiments were not a control to the conjugate experiments, but rather an additional, unplanned experiment suggested only after the initial conjugate tests were complete.

We note that this is not, as defendants have suggested, a "reduction to practice" case, whereby the named inventors conceived of the basic idea underlying the patent and the Weizmann scientists merely carried out the experiments to test Schlessinger's thesis. Although "the discovery that an invention actually works is part of its reduction to practice," Burroughs Wellcome, 40 F.3d at 1228, the Weizmann scientists alone conceived of the experiments that eventually led to the discovery of the synergistic phenomenon described in the 1988 paper and, later, the '866 patent. This is reflected not only in the testimony of the Weizmann scientists and in the documents corroborating their testimony, but also in the fact that the '866 patent extensively copies from the text and figures of the 1988 paper, which was entirely drafted by the Weizmann scientists.

In light of the extraordinary breadth of the evidence corroborating the inventorship claims of the Weizmann scientists, we conclude that Michael Sela, Esther Aboud-Pirak, and Esther Hurwitz have demonstrated by clear and convincing evidence that they are entitled to be named as inventors of the '866 patent. Collectively, they entirely conceived of the research project generating the data supporting the claims of the '866 patent, with Pirak and Hurwitz personally carrying out the experiments described in the patent. We now turn to the

question of whether the named inventors should be removed from the '866 patent.

2. The Named Inventors are Not Inventors of the '866 Patent[79]

i. Contribution of mAb 108 Insufficient for Inventorship

Defendants argue that "the selection of mAbs meeting the claim requirements is a significant contribution that requires that the named Rorer inventors remain as inventors." Def. Mem. of Law at 11 (emphasis and caps deleted). We disagree. Defendants' use of the word "selection" suggests that the named inventors made a conscious decision to give the Weizmann scientists antibodies with particular characteristics in anticipation of their being used in the way specified in the patent. The reality is that the creation of these antibodies

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[79] We note that defendants have argued that this Court should treat certain allegations in the original, unamended, complaint as admissions, specifically those statements that would suggest that defendants originally conceded joint inventorship. In light of the fact that plaintiff has come forward with a plausible rationale for amending the complaint, namely that they learned certain facts during discovery that revealed to them the lack of an inventive contribution by the defendants, see Tr. 1448 line 10 to 1449 line 8, we do not treat the allegations in the original complaint as concessions. See Shields v. CityTrust Bancorp, 25 F.3d 1124, 1128 (2d Cir. 1994) ("It is well established that an amended complaint ordinarily supersedes the original, and renders it of no legal effect.").

Moreover, in its answer in a parallel German case, Aventis stated that Schlessinger conceived of the '866 patent "at the end of 1985/beginning of 1986." PTS221T at 019. If that were in fact true, Schlessinger would still have been a full-time employee of the Weizmann at the time of conception, as he did not begin his sabbatical until March 4, 1986. See PTX027. Consequently, Schlessinger's role in the invention would belong to the Weizmann, not Meloy/Rorer. It is unclear from the record whether Aventis subsequently amended its answer in the German case.

had no causal relationship to the experimental models employed by the defendants. In fact, Schlessinger gave samples of the same antibodies to scientists at several institutions; at trial, there was no suggestion that he believed that each scientist to whom he gave mAbs 96 and 108 specified a need for antibodies with their particular characteristics.

More importantly, the '866 patent was drawn to a method for using antibodies in the same class as mAb 108, not to mAb 108 itself. As described supra, the PTO repeatedly and explicitly rejected claims drawn to mAb 108. The Supreme Court has explained that a PTO rejection "indicates that the patent examiner does not believe the original claim could be patented. While the patentee has the right to appeal, his decision to forgo an appeal and submit an amended claim is taken as a concession that the invention as patented does not reach as far as the original claim." Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd., 535 U.S. 722, 734 (2002) (citation omitted). Under the terms of its agreement with ImClone, Aventis had the right to continue pursuing a patent drawn to mAb 108, but declined to do so. If defendants had believed that they were entitled to a patent for mAb 108, they could have pursued obtaining one at the PTO. This Court, however, is not the appropriate forum in which to seek a patent, and we decline to revisit the PTO's numerous decisions not to grant such a

patent.[80]

Defendants' expert witness testified that mAb 108 was unique, as a "myriad of rearrangements . . . can occur in the human globulin gene." Tr. 1400 lines 15-16. Although this is true, the fact remains that at the time mAb 108 was created, there were several antibodies already in existence possessing the same three attributes described in Claim 1 of the '866 patent.[81] See Tr. 1293 line 19 to 1294 line 13. In fact, the antibody that ImClone has commercially developed and marketed under the name Erbitux is mAb 225, created in 1984 by Prof. Mendelsohn, well before Bellot began the process to create mAb 108. Consequently, whatever unique properties mAb 108 might possess, it is by no means the first antibody that fulfills the requirements of the '866 patent.

Ultimately, in order to establish entitlement to inventorship, defendants must do more than prove that the named inventors created the antibody used by the Weizmann scientists.

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[80] Moreover, the process by which mAb 108 was created was not in any way novel. Although Bellot suggested that her procedures were somehow unique, the Court was not presented with any documentary evidence to suggest that she significantly deviated from the method pioneered by Köhler and Milstein.

[81] We note that, to the extent that the defendants argue that the unique structure of mAb 108 is relevant to the issue of inventorship, its uniqueness derives from the cell line from which it was generated, namely the CH-71 cells taken from the Weizmann. Thus, even if we were to find that this is an issue of importance to the outcome, which we do not, the issue would not necessarily tip the scales in favor of the named inventors.

Although it might be the case that the Weizmann scientists would not have made their discovery if Schlessinger had not offered them mAb 108, "but for" causation is not tantamount to invention. We reiterate that "[c]onception is the touchstone of inventorship, the completion of the mental part of invention." Burroughs Wellcome, 40 F.3d at 1227-28. The proper inventors of the '866 patent are those who conceived of the idea of using mAb 108 in an unconjugated mixture in order to treat human tumor cells. This idea was the Weizmann scientists' alone.

ii. The Named Inventors did not Conceive of the Mixture Experiment

In light of our conclusion that the creation of mAb 108 does not per se entitle the named inventors to remain on the patent, defendants' remaining argument is that Schlessinger conceived of the research project performed at the Weizmann. As discussed below, this suggestion is wholly unsupported by corroborating evidence and cannot be credited.

Defendants rely on Burroughs Wellcome in suggesting that "Professor Schlessinger need not have communicated his complete conception to Dr. Hurwitz." Def. Mem. of Law at 39. This position is factually and legally flawed. First, defendants' argument presupposes that Schlessinger communicated any part of the invention to the Weizmann scientists, which, as discussed in the facts section, he did not do. Second, Burroughs Wellcome

does not support the notion that one person can conceive of an idea, keep it to himself, and then take credit for it before the Patent Office. In order to constitute conception, an "idea must be definite and permanent in the sense that it involves a specific approach to the particular problem at hand." Burroughs Wellcome, 40 F.3d at 1230. Thus, Burroughs Wellcome, and all of the other cases cited by defendants, requires proof of corroboration. See id. at 1229-30 ("[W]e [do not] suggest that a bare idea is all that conception requires. . . . And, of course, the alleged conception must be supported by corroborating evidence.") Here, not only was any idea Schlessinger might have had about the potential uses of mAb 108 far too indefinite to constitute conception, but there is also no corroborating evidence to suggest that Schlessinger did in fact contemplate the mixture experiment performed by the Weizmann scientists. Moreover, Schlessinger certainly did not specifically contemplate each of the decisions made by the Weizmann scientists during the fourteen months of experimentation that predated the discovery that forms the basis for the invention. Our inquiry is not what Schlessinger believed the Weizmann scientists might do with his antibodies, but rather whether he first conceived of the invention in a sufficiently definite manner. We find that he did not.

A brief discussion of Univ. of Colo. Found. v. American Cyanamid Co., 105 F.Supp.2d 1164 (D. Colo. 2000) ("Cyanamid"), aff'd, 342 F.3d 1298 (Fed. Cir. 2003), is instructive on this point. In Cyanamid, the University of Colorado was the assignee of the intellectual property rights of two of its professors, Dr. Robert Allen and Dr. Paul Seligman (the "Doctors"). Cyanamid, the manufacturer of a prenatal supplement, commissioned the Doctors to compare the iron absorption of its product with that of a competitor's product. After the Doctors determined that Cyanamid's product was "slightly better," they decided to do further research because neither product they tested provided the recommended amount of iron absorption. See id. at 1167. The decision to conduct further research was entirely the Doctors'. In their follow-up studies, the Doctors determined that "the large amounts of calcium carbonate and magnesium oxide" in Cyanamid's supplement "was inhibiting iron absorption," such that reformulating the product could "reduce or eliminate this effect." Id. The Doctors reported this conclusion to Cyanamid, which set to work on reformulating its supplement. The Doctors, meanwhile, drafted an article for publication, and, as a courtesy, sent an advance copy to Dr. Leon Ellenbogen, a personal friend and professional colleague who served as Cyanamid's chief chemist. The article clearly credited the Doctors alone for the experiments it described.

Upon receipt of the article, and as the named inventors did here, Dr. Ellenbogen "[n]evertheless . . . filed a Cyanamid company form called a 'Record of Inventorship' claiming inventorship of" the reformulated product. Id. at 1169.

The parallels continue. Immediately thereafter, Cyanamid began seeking a patent for the new product in Dr. Ellenbogen's name. Its patent application "copied significant portions of" the Doctors' article, including a table and four figures it contained. See id. at 1169. As the District Court found, "[t]he patent application, quite simply, is derived virtually wholesale from the [a]rticle." Id. at 1178. The Court continued:

> Notwithstanding the Doctors' personal and professional relationship with Dr. Ellenbogen . . . neither Dr. Ellenbogen nor Cyanamid mentioned anything about the patent application, the filing of an affidavit in support of it crediting Dr. Ellenbogen with instigating and supervising all of the studies, the issuance of the Patent itself, the award given Dr. Ellenbogen for being named the inventor on a successful patent, or the six civil enforcement actions brought by Cyanamid to prevent generic drug companies from using the patented technology.

Id. at 1169. Moreover, the Doctors only learned of the patent when "Dr. Ellenbogen inadvertently let the information slip in a 1993 conversation with Dr. Seligman over dinner." Id. The District Court held, and the Federal Circuit affirmed, that the

Doctors were the sole inventors of the issued patent, which was ordered corrected pursuant to 35 U.S.C. § 256.[82] Id. at 1186. The Court specifically rejected Cyanamid's assertion of joint inventorship, finding that "[t]he definite and permanent idea of the complete and final invention was exclusively that of the Doctors, and they are the true and sole inventors of the subject matter of the" issued patent. Id. at 1183.

Cyanamid is strikingly on point here, and wholly undermines the defendants' suggestion that the fact of creating mAb 108 and giving it to the Weizmann scientists somehow entitles the named inventors to remain on the patent. Like the Cyanamid court, we conclude that the plaintiffs have overcome the "presumption of correctness" that applies to issued patents. Cyanamid, 105 F.Supp.2d at 1182. Similarly, we conclude that the defendants have offered "no other evidence besides the testimony of" the named inventors "either to refute [p]laintiff's evidence or to prove that" Dr. Schlessinger and his colleagues "conceived of the patented invention." Id. The Federal Circuit requires evidence to corroborate a purported inventor's testimony in order to avoid the "tempt[ation] to remember facts favorable to [the inventor's] case by the lure of protecting [his] patent or defeating another's patent." Mahurkar v. C.R. Bard, 79 F.3d

[82] The Court also found that the laches defense was inapplicable, a finding we discuss infra.

1572, 1577 (Fed. Cir. 1996). Here, as in Cyanamid, the named inventors' testimony regarding conception is wholly uncorroborated. Consequently, they cannot be considered the inventors of the '866 patent.

iii. The Named Inventors are Not Joint Inventors

Moreover, the named inventors are not joint inventors. As we explained earlier in describing the relevant legal standard, joint inventorship requires "some element of joint behavior, such as collaboration or working under common direction, one inventor seeing a relevant report and building upon it or hearing another's suggestion at a meeting." Kimberly-Clark, 973 F.2d at 917. As our findings of fact make clear, there is no creditable evidence suggesting that the named inventors ever made any suggestions to the Weizmann scientists during their research or in any other way influenced the course of their experiments. In light of the absence of any evidence of collaboration, we find that the named inventors did not "contribute in some significant manner to the conception or reduction to practice of the invention." Pannu, 155 F.3d at 1351.

iv. Defendants are Judicially Estopped from Arguing that Figure 1(B) does not Disclose Element (iii)

During the course of their patent prosecution, defendants specifically represented to the PTO that Figure 1(B) of the 1988

paper, which they copied into the patent application, discloses element (iii) of Claim 1 of the '866 patent, which states, "wherein the antibody inhibit [sic] the binding of EGF to the EGF receptor." U.S. Patent 6,217,866. They now take the position that Figure 1(B) does not disclose Element (iii) in arguing that they must be considered at least joint inventors of the patent because they solely conceived of Element (iii). However, because the PTO adopted their argument that Figure 1(B) supports Element (iii), we conclude that defendants are judicially estopped from now arguing that the Weizmann scientists did not disclose Element (iii) in the 1988 paper.

The Supreme Court has explained that "where a party assumes a certain position in a legal proceeding, and succeeds in maintaining that position, he may not thereafter, simply because his interests have changed, assume a contrary position, especially if it be to the prejudice of the party who has acquiesced in the position formerly taken by him." New Hampshire v. Maine, 532 U.S. 742, 749 (2001) (quoting Davis v. Wakelee, 156 U.S. 680, 689 (1895))(internal quotation marks omitted). The Supreme Court explains further that the rule "generally prevents a party from prevailing in one phase of a case on an argument and then relying on a contradictory argument to prevail in another phase." New Hampshire, 532 U.S. at 749 (quoting Pegram v. Herdrich, 530 U.S. 211, 227, n. 8 (2000))

(internal quotation marks and additional citations omitted). The Second Circuit has stated, "The purposes of the doctrine are to preserve the sanctity of the oath and to protect judicial integrity by avoiding the risk of inconsistent results in two proceedings."[83] Mitchell v. Washingtonville Cent. Sch. Dist., 190 F.3d 1, 6 (2d Cir. 1999)(internal quotations omitted).

The doctrine of judicial estoppel squarely applies to the arguments now advanced by defendants. Defendants contend that the PTO did not "adopt[] the allegedly inconsistent position in some manner,"[84] Def. Mem. of Law at 59, suggesting that the PTO might have ignored the citation to Figure 1(B) and relied only on defendants' other citations. We do not credit this suggestion. The PTO adopted the defendants' argument that mAb 108 inhibits the binding of EGF to EGFR based upon defendants' reference to Figure 1(B), and there is no evidence in the record to suggest that the PTO only believed that certain of the defendants' citations supported their assertion. It is thus clear that: (1) the defendants argued that Figure 1(B) demonstrates that mAb 108 inhibits the binding of EGF to EGFR; and (2) the PTO adopted that position. In light of the fact

[83] Because this issue is a procedural one, Second Circuit law, rather than Federal Circuit law, applies. See, e.g., Lampi Corp. v. Am. Power Prods., Inc., 228 F.3d 1365, 1377 (Fed. Cir. 2000).

[84] Defendants use the word "allegedly" in their brief despite the fact that they vociferously argue that Figure 1(B) does not disclose Element (iii).

that defendants have already obtained the benefit of arguing that Figure 1(B) supports Element (iii) by virtue of obtaining the '866 patent, we will not permit defendants to argue now that their assertions to the PTO were incorrect.[85]

v. The Cases Relied Upon by Defendants are Unavailing

Both during oral argument and in their post-trial brief, defendants cited to a number of Federal Circuit cases that they believe support the named inventors' claims of inventorship. We specifically discuss several of these cases below in order to demonstrate that, in fact, they both undermine defendants' arguments and support plaintiff's claims of inventorship. Moreover, these cases provide insight into how the somewhat abstract idea of inventorship is interpreted by the Federal Circuit when it is presented with a tangible set of facts.

Linkow v. Linkow

At oral argument, Aventis' counsel suggested that Linkow v. Linkow, 517 F.2d 1370 (CCPA 1975), supported defendants' case because it demonstrated that a party challenging inventorship "cannot meet [its] burden based upon [an] article." Tr. 1510 line 19. Specifically, Aventis' counsel argued that Linkow

[85] In light of the testimony of Pirak and Lippmann, as well as the fact that defendants did, at least at some point, believe that Figure 1(B) discloses Element (iii), were we compelled to make a factual finding on what Figure 1(B) discloses, we would find that it does in fact disclose Element (iii). In so finding, we would acknowledge the closeness of this question as well as the fact that reasonable scientific minds are in disagreement.

requires the plaintiffs to proffer more evidence than just their published articles to prove conception of the claims embodied in the '866 patent.

Defendants' reliance on Linkow is misplaced. Unlike the present case, Linkow involved a party challenging inventorship relying solely on his own uncorroborated testimony. The Linkow plaintiff sought to have his name added to the defendant's patent under a joint inventorship theory based solely on his own recounting of the conversation that led to creation of the invention at issue. The Federal Circuit ruled for the defendant, finding that "the uncorroborated testimony of joint inventors is [not] sufficient to establish the fact of joint inventorship." Id. at 1373. In light of the overwhelming documentary evidence to substantiate plaintiff's claims of inventorship in the present case, Linkow is simply inapplicable.

Pannu v. Iolab Corp.

Defendants also rely on Pannu v. Iolab Corp., 155 F.3d 1344 (Fed. Cir. 1998), a patent infringement action in which the defendant claimed that it had not infringed the plaintiff's patent because, inter alia, the patent did not name all of the inventors. The Federal Circuit ruled that the district court erred in granting judgment as a matter of law in favor of plaintiff on the inventorship issue, finding that Iolab had raised issues of fact regarding the contribution to conception

made by a person not named on the patent. Defendants here argue that Pannu supports its claim to at least joint inventorship in light of that court's conclusion that the purported inventor had offered "sufficient evidence for a reasonable jury to find that Link was an actual inventor." Id. at 1351.

Pannu, however, also does not support defendants' claims to inventorship. In finding that Iolab had offered substantial evidence of improper inventorship, the court noted that the person named on the patent had corroborated the testimony of the person who claimed that he was deserving of inventorship status. Specifically, the Court noted that Pannu, the man named on the patent, conceded that Link, the man claiming to be a joint inventor, had contributed to the idea of using a one-piece construction for an artificial lens intended to replace a failed natural lens in human eyes. In Pannu, the lens itself was the subject of the patent; thus, a contribution to the conception of how to construct the lens could give rise to a claim of inventorship. Here, however, the named inventors' claim to joint inventorship is, in effect, premised on the contribution of one of the raw materials that gave rise to the patent for a method of that material's use. Just as the creators of doxorubicin and cisplatin, the two anti-cancer drugs referenced in the dependent claims, are not entitled to be named as inventors on the '866 patent, Schlessinger and his colleagues at

Meloy/Rorer are not entitled to inventorship simply because they created mAb 108.

Ethicon, Inc. v. U.S. Surgical Corp.

Defendants also argue that Ethicon, Inc. v. U.S. Surgical Corp., 135 F.3d 1456 (Fed. Cir. 1998) supports their claims to inventorship. Ethicon affirmed a district court decision adding an intervenor's name to a patent for a trocar, a surgical tool used in endoscopic surgery. Despite its finding of joint inventorship, the facts of Ethicon actually support a finding of sole inventorship for the Weizmann defendants.

In Ethicon, Dr. Yoon, the man who obtained the patent originally, began working on a safer trocar that would result in fewer injuries during surgery. Subsequently, he consulted with Choi, an electronics technician who intervened in the action, on creating the trocar. After their consulting arrangement ceased, Yoon filed for a patent for the trocar without informing Choi. The district court found, and the Federal Circuit affirmed, that Choi had made specific contributions to certain claims of the patent. Namely, Choi conceived of a method for constructing the trocar such that it would work in the manner Yoon intended. In order to corroborate his claim to co-inventorship, Choi produced contemporaneous sketches demonstrating that he, not Yoon, had conceived of certain elements of the patented device. In short, the court found that Choi "was presenting ideas to Yoon as the

sketches were drawn, rather than the other way around." Id. at 1464. Moreover, Yoon lacked the technical expertise to create the trocar himself, such that he was unable to fully conceive of the device without the help of someone with the sort of technical expertise possessed by Choi.

On its facts, then, Ethicon does not support the named inventors' arguments. In Ethicon, Choi not only partly conceived of elements of the independent claims of the patent, he also offered documentary evidence in the form of dated sketches substantiating the extent of his contribution. Here, however, defendants have offered testimony that Schlessinger thought of some of the elements of the independent claims, but have not offered any corroborating evidence to suggest that he ever communicated any of those thoughts to the Weizmann scientists, who solely conceived of the research project and testing protocol that led to the discovery underlying the '866 patent.

Burroughs Wellcome v. Barr Labs., Inc.

Despite defendants' reliance on Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223 (Fed. Cir. 1994), it presents almost precisely the opposite factual scenario from this case. Burroughs Wellcome arose after defendant Barr Laboratories sought FDA approval to market a generic version of AZT, a drug for which plaintiff held six patents relating to its

effectiveness in treating HIV and AIDS. As part of the application process for its generic drug, defendant Barr certified to the FDA that the plaintiff's patents were either invalid or were not infringed by the proposed generic drug. Plaintiff then filed an infringement action; Barr and its co-defendant Novopharm filed a counterclaim seeking to have two NIH scientists, Samuel Broder and Hiroaka Mitsuya, added to the six patents as co-inventors. The district court held entirely for the plaintiff/patentee (the "Burroughs scientists"), and the Federal Circuit affirmed in part and reversed in part, finding that although the plaintiff had demonstrated that the scientists named on the patents had solely conceived of those patents relating to the discovery that AZT was effective against HIV, there remained an issue of fact as to whether the two NIH scientists were co-inventors of the subject matter of the patent involving the use of AZT to increase the white blood cell count of people infected with HIV.

A close inspection of Burroughs Wellcome reveals extraordinary differences between its facts and the facts here, undermining the named inventors' claims to inventorship. In Burroughs Wellcome, the Burroughs scientists explicitly set out to find a treatment for HIV and AIDS. They began their research

by screening compounds for antiretroviral activity[86] when tested against two murine retroviruses, a leukemia virus, and the Harvey sarcoma virus. Thus, unlike the named inventors here, the Burroughs scientists' explicit goal in creating their compounds was to find an effective treatment against HIV. Then, after determining that AZT and some other compounds might prove effective in HIV therapy, the Burroughs scientists provided samples of their compounds to the NIH scientists with the explicit understanding that the NIH scientists would perform tests to determine how effective the compounds were against live HIV, which virus the Burroughs scientists did not possess. Again, this is in stark contrast to the facts here, as the Burroughs scientists had already determined the potential effectiveness of their compounds before they explicitly sought out the NIH scientists. Moreover, the Burroughs scientists and the NIH scientists reached a clear understanding of the type of testing that would be performed, as reflected by a dated letter sent by one of the Burroughs scientists to one of the NIH scientists. Further, the Burroughs scientists drafted a patent application for the use of AZT to treat HIV before they received the results of the testing performed by the NIH scientists, reflecting their clear expectation that the testing at the NIH would demonstrate AZT's therapeutic value. Here, the named

[86] I.e., effective against retroviruses like HIV.

inventors drafted a patent application after obtaining an advance copy of a draft paper written by the Weizmann scientists, reflecting results the Weizmann scientists observed after running more than a year's worth of different types of experiments. In contrast, the NIH reported its results to the Burroughs scientists about two weeks after receiving the AZT samples. See id. at 1230 ("[T]he testing was brief, simply confirming the operability of what the draft application disclosed."). Only after the initial patent application was filed and the FDA approval process was underway did the NIH scientists discover that AZT was also effective in increasing the T-cell (a type of white blood cell) count of HIV patients.

In affirming the district court's finding that the Burroughs scientists solely conceived of using AZT as an HIV therapy, the Federal Circuit explained that the Burroughs scientists were not required to prove that AZT would be effective against HIV in order to prove conception, but rather needed to prove only that they conceived of the idea of treating HIV with AZT with enough specificity such that "one skilled in the art" could practice the invention. See id. at 1230. Specifically, the court emphasized that the Burroughs scientists "had thought of the particular antiviral agent with which they intended to address the problem, and had formulated the idea of the inventions to the point that they could express it clearly

in the form of a draft patent application," which specifically disclosed "the intended use of AZT to treat AIDS." Id. Consequently, the Burroughs scientists "had more than a general hope or expectation" that AZT would prove to be effective as a therapeutic agent. Id. The Court concluded that the draft patent shows "that the idea was clearly defined in the inventors' minds; all that remained was to reduce it to practice – to confirm its operability and bring it to market." Id.

The Federal Circuit, however, reversed the district court's finding that the Burroughs scientists were the sole inventors of the patent related to AZT's use in increasing T-cell count, concluding that there was a triable issue of fact regarding whether a scientist skilled in the art "would . . . have expected T-cell count to rise." Id. at 1232. Specifically, the Court suggested that the increase in T-cell count might not be an obvious consequence of AZT's antiretroviral effect, such that a jury might reasonably conclude that the NIH scientists conceived of this specific invention, embodied in a separate patent. Significantly, the Court pointed out that, even though one might conclude that this effect was obvious and might have in fact been known by the Burroughs scientists, the court is required to assume each of the six patents is "drawn to an invention different from each of the other five patents." Id. at 1232, n.8. The court stated that the issue presented was not

"whether one skilled in the art could have thought of the invention, but whether the alleged inventors had in their minds the required definite and permanent idea." Id. at 1232 (citation omitted). Thus, the partial reversal in Burroughs Wellcome was premised on the lack of proof offered by the Burroughs scientists that they actually conceived of one of the patents; similarly here, the named inventors have not offered any proof of actual conception of the ideas embodied in the '866 patent.

Fina Oil and Chemical Co. v. Ewen

In Fina Oil and Chemical Co. v. Ewen, 123 F.3d 1466 (Fed. Cir. 1997), the Federal Circuit held that a district court improperly granted summary judgment in favor of one purported inventor of a patent disclosing a "metallocene catalyst used to produce syndiotactic polypropylene (SPP) and methods for making the catalyst." Id. at 1468. Like this Court, the Fina Court was presented with two parties each claiming sole inventorship of an issued patent. Fina was the assignee of the patent rights of Dr. Abbas Razavi, whose experiments resulted in the catalysts disclosed in the issued patent. Fina brought an action seeking a declaration that Dr. Razavi was the sole inventor of the patent; the defendant, Dr. John Ewen, was Razavi's supervisor during the period when the invention was created. The PTO had

previously issued the patent to Razavi and Ewen as co-inventors.[87]

In reversing the decision granting summary judgment to Razavi, the Federal Circuit held that the district court improperly applied the doctrine of simultaneous conception and reduction to practice, which provides that, in certain instances, "an inventor may only be able to establish a conception by pointing to a reduction to practice through a successful experiment." Id. at 1473. The Court reasoned that the district court had erred in using the doctrine to demonstrate that because Ewen "did not conceive or reduce to practice the entire claimed invention, he . . . did not at least contribute in some significant way to the ultimate conception." Id. at 1474. In finding that there were issues of fact regarding whether Ewen had made a substantial inventive contribution, the Fina Court cautioned that, "[t]he basic exercise of the normal skill expected of one skilled in the art, without an inventive act, does not make one a joint inventor." Id. at 1473 (citation omitted).

The doctrine of simultaneous conception and reduction to practice is inapplicable here, as it would have been possible to conceive of the invention without having actually demonstrated

[87] The reasons why Fina later sought a declaration that Razavi was the sole inventor are not relevant here, so we decline to discuss them.

its scientific viability.[88] Here, conception occurred when Hurwitz suggested the mixture experiment; its reduction to practice was not the conceptual act itself, but rather validated Hurwitz's intuition that a mixture might prove to be more therapeutically beneficial than a conjugate.

Thus, although the doctrine is inapplicable as a matter of law, its underlying rationale helps explain why the named inventors cannot be credited with a conceptual act simply because they provided the Weizmann scientists with the antibody.

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[88] The Burroughs Wellcome Court explained the application of the doctrine is as follows:

> It is undoubtedly true that "[i]n some instances, an inventor is unable to establish a conception until he has reduced the invention to practice through a successful experiment." Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1206 (Fed. Cir. 1991). But in such cases, it is not merely because the field is unpredictable; the alleged conception fails because . . . it is incomplete. Then the event of reduction to practice in effect provides the only evidence to corroborate conception of the invention.
>
> Under these circumstances, the reduction to practice can be the most definitive corroboration of conception, for where the idea is in constant flux, it is not definite and permanent. A conception is not complete if the subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete invention as it will be used in practice. It is this factual uncertainty, not the general uncertainty surrounding experimental sciences, that bears on the problem of conception.

Burroughs Wellcome, 40 F.3d at 129 (internal citations omitted).

The idea to test a mixture of a monoclonal antibody and a chemotherapy drug against cancer cells mitogenically stimulated by EGF resulted from the experiments performed at the Weizmann, and was the Weizmann scientists' idea alone. Unlike in Fina, where the Federal Circuit found that issues of fact precluded summary judgment, the named inventors had no supervisory capacity over the Weizmann scientists. In fact, the situation was quite the opposite; Schlessinger in no way directed the research of the Weizmann scientists and had absolutely no interaction with them during the course of their experimentation. Fina thus does not offer the named inventors any support.

IV. The Laches Defense is Inapplicable

Defendants argue that the legal doctrine of laches bars plaintiff's claims in light of the fact that this lawsuit was initiated more than a decade after defendants first submitted an application for a patent. As discussed below, we reject the laches defense, as defendants willfully engaged in a course of conduct that prevented plaintiff from learning about their patent applications.

A. Legal Standard

The affirmative defense of laches applies when: (1) a plaintiff unreasonably delays bringing suit; and (2) the delay results in material prejudice to a defendant. See A.C. Aukerman

Co. v. R.L. Chaides Const. Co., 960 F.2d 1020, 1028 (Fed. Cir. 1992)(en banc). Laches is an equitable defense, and is thus committed to the "sound discretion of the trial judge." Id. "When applying the equitable doctrine of laches in order to bar a claim, the period of delay is measured from when the claimant had actual notice of the claim or would have reasonably been expected to inquire about the subject matter." Advanced Cardiovascular Sys. v. SciMed Life Sys., Inc., 988 F.2d 1157, 1163 (Fed. Cir. 1993). The Federal Circuit applies the "knew-or-should-have-known criterion" in measuring when a plaintiff should be charged with inquiry notice of a legal right. Id. at 1162.

1. Yeda did not Unreasonably Delay Bringing Suit

Because we find that defendants' hands are unclean, i.e., they are responsible for plaintiff not finding out about their patent applications, the laches defense is unavailable to defendants. The conclusion of the Cyanamid court that the laches defense is barred where the delay in discovering a patent application "was the result of the very conduct for which relief is sought" is equally applicable here. Univ. of Colo. Found., Inc. v. American Cyanamid Co., 974 F.Supp. 1339, 1355 (D.Colo. 1997) rev'd on other grounds, 196 F.3d 1366 (Fed. Cir. 1999), remanded to 974 F.Supp. 1339, aff'd, 342 F.3d 1298 (Fed. Cir. 2003). Here, the defendants began seeking a patent in 1988, but

plaintiff did not become aware that defendants were seeking a patent until 2000, the '866 patent did not issue until 2001, and plaintiff did not locate the patent until 2002. Between the time Yeda located the issued patent and brought suit, they engaged in a series of discussions with defendants in an attempt to settle this matter out of court. After those efforts failed, Yeda filed suit in late 2003. We will not reiterate the extraordinary lengths defendants undertook to prevent the named inventors from discovering their actions. These are fully set forth in the facts section. Rather, we simply note that defendants could have contacted Yeda and discussed the inventorship issue at any time in the period from 1988 to 2000. Instead, they engaged in a series of actions designed to keep Yeda and the Weizmann scientists in the dark. Put simply, in light of their own misconduct, defendants may not complain now of plaintiff's failure to bring suit earlier. We do not doubt that if Yeda had become aware of the patent application earlier, they would not have hesitated to assert their legal rights.[89]

[89] Defendants argue that Yeda "should have taken reasonable steps to monitor public patent activity . . . ." Def. Mem. of Law at 41. While it might be true that Yeda could have invested greater resources in tracking patent applications, we decline to charge it with an obligation to do so. There is simply no legal obligation to track patent applications in order to prevent other scientists from claiming credit for one's own work.

2. Defendants were Not Prejudiced

Although we conclude that plaintiff did not unreasonably delay bringing suit, obviating the need to discuss the second prong of the laches defense, we note that any prejudice suffered by defendants is of their own doing, and is thus not a valid reason to permit the laches defense. As discussed in the fact section, ImClone spent the vast majority of its funds investing in Erbitux after it became aware of the inventorship dispute. See Hemstreet v. Computer Entry Sys. Corp., 972 F.2d 1290, 1294 (Fed. Cir. 1992) (stating that the change in position "must be because of and as a result of the delay, not simply a business decision to capitalize on a market opportunity.") (citing Aukerman, 960 F.2d at 1033). Had the defendants simply put Yeda on notice of its intention to file a patent in 1988, there would have been absolutely no risk of prejudice. We now decline to employ an equitable tool to prevent plaintiff from obtaining those legal rights that defendants attempted to conceal from Yeda for over a decade.

CONCLUSION

For the reasons discussed above, we find that plaintiff has demonstrated by clear and convincing evidence that Drs. Michael Sela, Esther Aboud-Pirak and Esther Hurwitz are the sole inventors of the '866 patent and that laches does not bar plaintiff's claims. Consequently, pursuant to 35 U.S.C. § 256,

we order the Director of the Patent and Trademark Office to issue a certificate correcting the '866 patent, such that Drs. Sela, Pirak and Hurwitz are the only names appearing thereon.

IT IS SO ORDERED.

Dated: New York, New York
September 18, 2006

NAOMI REICE BUCHWALD
UNITED STATES DISTRICT JUDGE

NAOMI REICE BUCHWALD
UNITED STATES DISTRICT JUDGE

Copies of the foregoing Opinion and Order have been mailed on this date to the following:

Counsel for Plaintiff
Nicholas P. Groombridge, Esq.
Daniel J. Melman, Esq.
Jeannie Karl, Esq.
Michael A. Epstein, Esq.
Weil, Gotshal & Manges LLP
767 Fifth Avenue
New York, NY 10153

Counsel for Defendant ImClone
George E. Badenoch, Esq.
Richard L. DeLucia, Esq.
John W. Bateman, Esq.
Kenyon & Kenyon
One Broadway
New York, NY 10004

Counsel for Defendant Aventis
Jeffrey I. D. Lewis, Esq.
Karla G. Sanchez, Esq.
Irene Choi, Esq.
Patterson Belknap Webb & Tyler
1133 Avenue of the Americas
New York, NY 10036